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Assessment of myocardial ischemia in borderline coronary artery lesions based on optical pumped magnetometer magnetocardiography

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1	Assessment of myocardial ischemia in borderline coronary artery lesions based on optical pumped
2	magnetometer magnetocardiography
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20	Disclosures : The authors have nothing to disclose.
21	
22	Abstract

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Aims: Despite clinical guideline recommendations for its use, the uptake of fractional flow reserve (FFR) in borderline coronary artery lesions remains low. As a noninvasive and safe test for myocardial ischemia, the validity of optical pumped magnetometer magnetocardiography (OPM-MCG) versus invasive FFR has not been fully established. Methods and Results: A total of 141 stable patients with borderline coronary artery lesions were prospectively enrolled from June 30 to November 30, 2023. All of them underwent sequential OPM-MCG before invasive coronary angiography and FFR. Six parameters were included in the final diagnostic model: MAg_{max}-TT, CAg_{max}-TT, δ Ag_{sum}-C, δ Ps_{sum}-PP, δAr_{sum} -N and RtoAr_{max}-PN. 500 bootstrap replications showed that the area under the receiver operating characteristic curve 95% confidence interval of the diagnostic model was 0.841 (0.804-0.844), with sensitivity of 76.5%, specificity of 91.8%, positive predictive value of 89.7%, negative predictive value of 80.7%. 1000 bootstrap replications showed that the model was well-calibrated. There is a net clinical benefit of using the MCG ischemia diagnostic model for borderline coronary lesions if the threshold probability of patients is greater than 12%. Conclusion: A nomogram based on 6 OPM parameters was built to assess myocardial ischemia in borderline coronary artery lesions and can reduce unnecessary invasive examination. **Keywords:** borderline coronary artery lesions; optical pumped magnetometer magnetocardiography; fractional flow reserve; myocardial ischemia Introduction

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Borderline coronary lesions have stenosis ranging from 40% to 90% as seen in invasive coronary
angiography. The FAME study ^[1] found that over 80% of lesions fell into this category, with only 35%
of stenoses between 50-70% being hemodynamically significant. Predicting relevance was most

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accurate when estimating coronary artery diameter over 90%. The ongoing debate stems from the 2021
 ACC/AHA/SCAI Guidelines for Coronary Artery Revascularization ^[2] indicating uncertainty
 regarding the advantages of coronary interventions in patients with nonischemic borderline lesions.

T Fractional flow reserve (FFR) guided intervention in patients with borderline coronary artery lesions (40-90% stenosis) has become a recommended treatment strategy in the 2018 ESC Interventional Guidelines ^[3]. The 2021 ACC/AHA/SCAI Guidelines for Coronary Artery Revascularization also have clear recommendations for borderline lesions: FFR and instantaneous wave-free ratio (iFR) are used to assess the need for percutaneous coronary intervention (PCI) in patients without evidence of ischemia but with angina and other equivalent symptoms (Class I); PCI is not recommended for stable patients with FFR >0.8 or iFR >0.89 (Class III). FFR is considered the benchmark for detecting ischemia in such situations. However, its widespread adoption in coronary catheter laboratories is hindered by its time-consuming nature, consumption of resources, and potential adverse effects associated with adenosine application.

Optical pumped magnetometer magnetocardiography (OPM-MCG) measures tiny magnetic fields (10⁻¹⁵ Tesla) from the heart using atomic magnetometer technology, without radiation. It's quick, contactless, and suitable for diverse populations. Clinical studies have shown that MCG is better than electrocardiogram (ECG) at detecting early myocardial ischemia ^[4,5,6] and has similar diagnostic effectiveness as SPECT for coronary artery disease (CAD) ^[7,8]. MCG is precise in diagnosing non-ST-segment elevation myocardial infarction, even in individuals who do not exhibit typical angina. ^[9,10]. However, the use of MCG for assessing myocardial ischemia in borderline coronary artery lesions still needs to be established.

Hence, this study aims to investigate the accuracy of OPM-MCG in diagnosing myocardial

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67	ischemia in patients with borderline coronary lesions, with invasive FFR examination serving as the
68	reference standard.
69	
70	Method
71	Study population
72	This study was a prospective, single-center, observational, cohort study which was reviewed by the
73	Ethics Committee of Beijing Anzhen Hospital, Capital Medical University, and registered with the
74	China Clinical Trial Registry (ChiCTR2300072382). All participants signed an informed consent. The
75	methods described in this article follow the STARD 2015 guidelines.
76	Participants aged 18-80 with typical angina symptoms (CCS class II or higher) or 40-90% stenosis
77	on CCTA were scheduled for hospitalization for invasive coronary angiography (ICA). Exclusion
78	criteria included: 1) Coronary artery stenosis outside of 40%-90% range on ICA; 2) Acute myocardial
79	infarction; 3) Previous myocardial infarction; 4) Complex arrhythmias; 5) Bundle-branch block; 6)
80	Pacemakers, metallic implants in trunk; 7) Claustrophobia.
81	Sample size was calculated by PASS 2021 software. This study was a prospective cohort study,
82	and the area under the ROC curve was used for sample size calculation, taking the significance level (α)
83	as 0.025 and the degree of certainty $(1-\beta)$ as 0.90, combining the results of the literature review of related
84	studies as well as the statistics of the small sample in the previous period, and calculating according to
85	the FFR-positive (ischemic)/FFR-negative (non-ischemic)=2:3. The sample size was calculated as 138.
86	Between June 30 and November 30, 2023, patients who satisfied the inclusion criteria were
87	consecutively enrolled, resulting in a total of 163 participants being recruited for this study. 141 patients
88	with borderline coronary lesions underwent OPM-MCG and FFR assessments after excluding 22

patients for different reasons (Figure 1). In this study, the cardiologists were not aware of the MCG
results at the time of the FFR examination, and the MCG parameters were determined before the FFR
examination.

93 MCG imaging

MCG recordings were conducted using a 36-channel OPM-MCG system with atomic magnetometers (Miracle MCG, Beijing X-MAGTECH Technologies Ltd.). The sensitivity of the magnetometers is below 30fT/Hz1/2, and the residual magnetic field is kept below 5nT. Each subject had a 90-second continuous recording at 36 locations (6×6 grid) above the chest using an arrayed sensor grid. Once MCG data collection is complete, the software automatically generates precise magnetic field and current density maps and outputs their parameters (see Supplemental text for additional detail). The parameters and cut-off values of MCG that indicate myocardial ischemia are presently undefined, thus the current study is exploratory in its approach.

103 ICA and FFR procedures

104 Coronary angiography and FFR measurements were performed on the vessels according to the 105 2021 ACC/AHA/SCAI Guidelines for Coronary Artery Revascularization and Expert consensus on the 106 clinical pathway for FFR measurement in China. After administration of nitroglycerin, a pressure 107 monitoring guidewire was advanced through the stenosis. Hyperemia was attained by administration of 108 intravenous adenosine (140µg/kg/min). The FFR pressure wire was positioned a minimum of 20 mm 109 distal to the stenosis in vessel segments \geq 2 mm. The presence of an FFR \leq 0.80 was considered a positive 110 indicator of functional ischemia in patients and was defined as the FFR-positive group.

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6 7	112	Statistical Analysis
/ 8		·
9	113	Data analysis was performed with SPSS 26.0 and R 4.3.2 (http://www.R-project.org/) Counting
10		
11	11/	data ware presented as numbers and percentages, while normally distributed measurement data ware
12	114	data were presented as numbers and percentages, while normany distributed measurement data were
14	115	shown as mean 1 standard deviation. Continuous variables that were not normally distributed were
15	115	shown as mean \pm standard deviation. Continuous variables that were not normany distributed were
16	440	
1/ 18	116	presented using median and quartile values. Statistical significance was determined for all analyses with
19		
20	117	a P-value less than 0.05.
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22 23	118	
23 24		
25	119	Development and internal validation of the diagnostic model
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27	120	We used logistic regression and LASSO regression to select the most predictive variables from 65
28 29		
30	121	pre-selected potential candidate variables obtained based on OPM-MCG (see Supplementary Text for
31		
32	122	definitions and pre-selection of candidate variables). The optimal model was determined through cross-
33 34		
35	123	validation. We considered the number and reasonableness and evaluated the parameters for the
36	120	vandauton. We constanted the number and reasonables and evaluated the parameters for the
37	124	regression model and used multivariate logistic regression with the backward method to incorporate
38	124	regression model and used multivariate logistic regression with the backward method to meorporate
40	405	madiator variables. The modella madiative nonfermence was accord using the enhanced bestature.
41	125	predictor variables. The model's predictive performance was assessed using the enhanced bootstrap
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43	126	method and clinical benefit was evaluated using decision curve analysis. The MCG-FFR nomogram was
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46	127	used to report scores for assessing myocardial ischemia with OPM-MCG parameters.
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51	129	Result
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53 54	130	Clinical characteristics
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56	131	The study included 141 patients, mostly male (77.3%) with an average age of 60.64 ± 9.70 years.
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58	132	After MCG scans, all patients underwent ICA and FFR examination, with 48.2% having positive FFR
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133 (FFR ≤ 0.8). A total of 157 vessels were examined, with 47.1% having FFR ≤ 0.8 . Interval between 134 MCG and FFR less than 30 days, median 2 days. Most patients had FFR measurements primarily done 135 on the LAD. See Table 1 for patient clinical characteristics.

137 Selection of parameters and development of the diagnostic model

Fifty variables that were statistically significant (P < 0.1) in univariable logistic regression were included in the LASSO regression (Table 2 and Figure 2 in supplemental text), and eight variables were selected based on the reasonableness of the parameters selected to reduce the model overfitting and covariance through LASSO regression. By using the backward approach, six parameters were included in the final diagnostic model: MAg_{max}-TT, CAg_{max}-TT, δAg_{sum}-C, δPs_{sum}-PP, δAr_{sum}-N and RtoAr_{max}-PN. The model area under the receiver operating characteristic curve (AUC) obtained from multivariate logistic regression analysis was 0.87, with sensitivity of 76.5%, specificity of 91.8%, positive predictive value of 89.7%, negative predictive value of 80.7%. The nomogram (Figure 2) provides a graphical overview of the diagnostic model using multivariate logistic regression analysis (Table 3 in supplemental text).

149 Internal validation and net benefit of the model

The model performance for the diagnosis of myocardial ischemia in borderline coronary artery lesions of the OPM-MCG was evaluated by bootstrap replications.500 bootstrap replications showed that the model AUC and a 95% confidence interval (CI) of 0.87 (0.809-0.932) (Figure 3). 1000 bootstrap replications showed that the model was well-calibrated. The mean absolute error was 0.032 (Figure 3). The decision curve analysis (DCA) for the diagnostic model showed that if the threshold probability of

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3 4 5	155	patients is greater than 12% (Figure 3), screening strategies based on the OPM-MCG diagnostic model
6 7	156	resulted in superior net benefit than screen-none or screen-all strategies.
8 9 10	157	
11 12	158	Discussion
13 14 15	159	The feasibility of diagnosing myocardial ischemia in patients with borderline lesions using OPM-
16 17 18	160	MCG was shown in our study, when compared to invasive FFR. The collective diagnostic potential of
19 20	161	MCG parameters in detecting myocardial ischemia in borderline coronary artery lesions resulted in an
21 22 23	162	AUC of 0.87 (95% CI 0.809 to 0.932), comparable to a prior investigation conducted by Park JW et al
24 25 26	163	^[11] which found that ST-segment fluctuation scores had an AUC of 0.84. This study stands out as the
20 27 28	164	sole comparison between MCG and FFR for CAD utilizing a '64-channel axial gradiometer system.' In
29 30 31	165	the study by Park JW and colleagues, patients could only detect myocardial ischemia under stress
32 33	166	conditions, and the examination required a specialized shielded room. In contrast, OPM-MCG does not
34 35 36	167	require liquid helium cooling or a dedicated shielded room. It can accurately diagnose myocardial
37 38 39	168	ischemia caused by borderline coronary artery lesions even when the patient is at rest, presenting a
40 41	169	contrast to the previous study.
42 43 44	170	CAD is presently characterized by an epicardial vascular lesion with a stenosis exceeding 50% in
45 46 47	171	the ICA. Frequently, this description acts as a reference for heart muscle revascularization. Moreover,
48 49	172	FFR can be used to evaluate the existence of myocardial ischemia, with a threshold of 0.8. Numerous
50 51 52	173	studies ^[12,13] have consistently demonstrated that FFR-guided stenting leads to superior immediate
53 54	174	outcomes and long-term prognosis. Therefore, FFR carries a Class 1a recommendation for guiding
56 57	175	revascularization in angiographically borderline coronary stenoses in patients with stable angina.
58 59 60	176	However, as illustrated in the Figure 4, the coronary stenosis identified in ICA may not precisely align

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with the invasive FFR results. This observation is in line with the conclusions drawn in the 2019 ESC Guidelines for Chronic Coronary Syndromes ^[14,15], emphasizing that the accuracy of determining CAD solely based on angiographic stenosis was as low as 64% when compared to flow reserve fraction. The positive mismatch rate, where lesions with less than 50% stenosis may demonstrate an FFR ≤ 0.8 , was 19%, while the negative mismatch rate, where lesions with over 50% stenosis may result in an FFR value > 0.8, reached up to one-third. However, due to factors such as time consumption, costs, patient-related discomfort, contraindications, and a lack of reimbursement, the current rate of FFR utilization in catheterization laboratories in China is less than 6% [Error! Bookmark not defined.]. OPM-MCG allows ischemia assessment in patients with borderline coronary lesions prior to ICA and has a good concordance with invasive FFR.As a result, OPM-MCG can provide a basis for precise diagnostic and treatment strategies in patients with borderline coronary lesions before ICA, reducing unnecessary invasive testing.

The current non-invasive methods with high accuracy for myocardial ischemia assessment are SPECT, positron emission tomography/CT (PET/CT) and cardiac magnetic resonance imaging (CMR). However, due to the use of radioactive substances, tedious operation, high price, long examination time and waiting time for appointments, CMR (13.5%) and SPECT (12.9%) are not widely practiced ^[16]. In a prospective study done by Roel S. et al. ^[17] 2022, which included 189 patients in a head-to-head comparison, it was found that using FFR as the gold standard, the sensitivity of SPECT, PET/CT, and CMR was only 67%, 81%, and 66%, and the specificity was only 61%, 65%, and 62%. The diagnostic accuracy of PET/CT (75%) was not statistically different from that of SPECT (65%, P=0.03) and MRI (64%, P=0.052). In recent years, CT-derived fractional flow reserve (CT-FFR) has gradually developed into a new noninvasive test for detecting myocardial ischemia. The results of a multicenter study showed

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that the sensitivity of CT-FFR in diagnosing coronary myocardial ischemia was 89%, the specificity
was 91%, and the diagnosis was in good concordance with FFR ^[18]. However, CT-FFR still has obvious
limitations. Good image quality is essential for CT-FFR, but in this research, 13.9% of instances (58 out
of 418) were unable to calculate CT-FFR due to inadequate image quality and the intricate nature of the
coronary artery system. Additionally, CT-FFR cannot currently assess microvascular lesions (<2 mm in
diameter) and diffuse lesions ^[19].

Similar to previous studies ^[20,21], a positive MCG scan was demonstrated by one or more abnormalities in the TT segment, including changes in TT segment parameters and changes in image dipoles (non-dipole phenomena and angular deflection of currents or magnetic fields). Different MCG parameters and combinations of parameters can provide more incremental information on cardiovascular disease. MCG is capable of accurately diagnosing myocardial ischemia resulting from epicardial coronary artery disease as well as effectively detecting myocardial ischemia caused by coronary microvascular dysfunction (CMD). The accuracy of MCG identification of CMD is 94.8% $(\pm 6.4\%)$, sensitivity of 100% $(\pm 0.0\%)$, and specificity of 93.3% $(\pm 8.2\%)$ ^[22]. In our study, we also found a small number of FFR-negative patients with positive MCG scans as described above ^[23], and considered the possibility of CMD. In the future, we will summarize the characteristic images of patients with CMD and further explore the incremental information provided by the MCGs for these patients. OPM-MCG tackles the pain points of SQUID-based MCG and facilitates its promotion in the clinic. MCG is mainly divided into two types: superconducting SQUID-based MCG and OPM-MCG. Although the SQUID-based MCG was developed earlier, it requires liquid helium refrigeration to realize lowtemperature superconductivity and the construction of a large magnetic shielding room, which limits its

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220 large-scale popularization and use. The OPM-MCG can operate at room temperature without liquid

helium cooling ^[24]. Moreover, the MCG is equipped with a lightweight magnetic shielding system,
which enables it to realize high-sensitivity magnetic measurements while significantly reducing
equipment maintenance costs and providing more flexible application scenarios.

MCG has been proved to be in good concordance with FFR in the preoperative assessment of myocardial ischemia in patients with borderline coronary artery lesions, and more clinical information can be provided to patients with cardiovascular disease through more studies in the future. MCG is expected to be used for the preoperative assessment of lesion-specific ischemia in patients with borderline coronary arteries, and to reduce the number of unnecessary invasive coronary arteriography examinations. This will effectively reduce the pressure on national healthcare expenditures and reduce the burden on patients with cardiovascular diseases.

232 Limitation

The study is a single-center registry study with some limitations. There is a need for a multicenter, prospective study involving a larger patient population. There are many types of MCG, and the current method of analyzing the cardiac magnetic field for the Miracle MCG was not compared head-to-head with other equipment. This study was not further externally validated, and in the future we will further refine and explore the feasibility of myocardial ischemia by MCG parameters.

- 51 239 **Conclusion**

MCG shows good sensitivity, specificity, and diagnostic accuracy in identifying significant
 coronary artery disease when compared to FFR. More extensive future research is necessary to confirm
 the effectiveness of MCG as a non-invasive approach for diagnosing and assessing the ischemic

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3 4 5	243	condition of borderline coronary artery blockages. Therefore, MCG can provide the evidence for a
6 7	244	precise diagnostic strategy for patients with borderline coronary lesions before ICA, reducing
8 9 10	245	unnecessary invasive examination.
11 12 13	246	
14 15	247	Ethics approval and consent to participate
16 17 18	248	This study was performed in accordance with the principles of the Declaration of Helsinki. This study
19 20 21	249	was approved by the ethics committee of Beijing Anzhen Hospital, Capital Medical University
22 23	250	(KS2023008). Written informed consent was required for participation in the study.
24 25 26	251	
27 28 29	252	Competing interests
30 31	253	The authors declare that they have no conflicts of interest.
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48 49 50	260	
50 51 52	261	Author contribution
53 54 55	262	Xiantao Song, Chenchen Tu and Hongjia Zhang helped to conceive the topic and revised the article.
56 57	263	Shuwen Yang and Lanxin Feng wrote the manuscript. and finished the statistics, Mingduo Zhang, Min
59 60	264	Zhang, Jiqiang He, Yanlong Ren, Yawei Luo and Feng Xu contributed to the data collection. Zhao Ma,

2		
3 4 5	265	Huan Zhang, Yazhe Zhang, Linqi Liu, Shu Zhou, Xin Zhao, and Xueyao Yang helped with data analysis.
6 7	266	All authors read and approved the final manuscript .
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19 20 21	271	
21 22 23	272	Patient and Public Involvement
24 25 26	273	Patients make more people aware of the clinical role of the MCG and how it is examined by forwarding
27 28 20	274	news stories and sharing information about clinical studies with others
29 30 31	275	
32 33 34	276	Abbreviations
35 36	277	AUC= area under the receiver operating characteristic curve
37 38 39	278	CCTA= coronary computed tomography angiography
40 41 42	279	CI= confidence intervals
42 43 44	280	FFR= fractional flow reserve
45 46 47	281	ICA= invasive coronary angiography
48 49	282	NPV= negative predictive value
50 51 52	283	OPM-MCG= optical pumped magnetometer magnetocardiography
53 54 55	284	OR= Odds ratio
56 57	285	PPV= positive predictive value
58 59 60	286	ROC= receiver-operating characteristic

287
288 Availability of data and materials
289 The data that support the findings of this study are available on request from the corresponding author,
290 Xiantao Song, upon reasonable request.

292 Reference

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Table 1 Clinical characteristics ($n = 1$	141)
Characteristics	Total(n=141)
Age (yrs)	60.64±9.70
Male, n (%)	109(77.3)
BMI ª (Kg/m²)	26.15±3.36
Diabetes, n (%)	47(33.3)
Hypercholesterolemia, n (%)	65(46.1)
Hypertension, n (%)	82(58.2)
Stroke, n (%)	9(6.4)
Smoke, n (%)	43(30.5)
Systolic blood pressure, mmHg	128.69±15.54
Diastolic blood pressure, mmHg	75.15±10.79
Heart rate	73.81±10.38
Medication, n(%)	
Aspirin	129(91.5)
Statin	137(97.2)
ACEI/ARB ^b	45(35.6)
SGLT2 ° inhibitors	22(16.7)
Nicorandil	23(16.3)
Admission lab results	
Low-density lipoprotein cholesterol (mmol/L)	1.82±0.69

hs Tnl(pg/ml)	3.5(2.5,5.8)
Brain natriuretic peptide (pg/ml)	29.00(14.75,48.25
Blood glucose (mmol/L)	5.52(4.82,7.33)
HbA1c ^d (%)	6.25(5.7,7.1)
ICA ^e and FFR ^f characteristics	
1-vessel disease	50(35.5)
2-vessel disease	43(30.5)
3-vessel disease	48(34.0)
Number of patients with FFR≤0.8	68(48.2)
Number of vessels with FFR	157
Number of vessels with FFR≤0.8	74(47.1)
Left anterior descending artery with FFR	97(68.8)
Left circumflex artery with FFR	25(17.7)
Right coronary artery with FFR	35(24.8)
Interval between MCG and FFR	2(1,7)

Values are n (%) or mean \pm SD.;

a. BMI= Body Mass Index; b. ACEI= angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; c. SGLT2 inhibitors = sodium-glucose cotransporter-2 inhibitors; d. HbA1c= glycated hemoglobin; e. ICA = invasive coronary angiography; f. FFR = fractional flow reserve.

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Figure legend

Figure 1. Flowchart of the study design.

Figure legend : CCTA= coronary computed tomography angiography; MCG=magnetocardiography; ICA= invasive coronary angiography; FFR=fractional flow reserve; PCI= percutaneous coronary intervention.

Figure 2. Nomogram of the diagnostic model.

Figure legend: The nomogram graphically demonstrates the diagnostic model of OPM-MCG. Points for MAg_{max} -TT, CAg_{max} -TT, δAg_{sum} -C, δPs_{sum} -PP, δAr_{sum} -N and $RtoAr_{max}$ -PN can be obtained using a point caliper and then summed to obtain a total score that can be obtained using a point caliper and then summed to obtain a total score that can be measured with diagnosing myocardial ischemia in patients with borderline coronary lesions.

Figure 3 Accuracy and internal validation of the diagnostic model.

Figure legend: (A) ROC curves and 95% confidence intervals. After 500 bootstrap replications, the area under the curve and 95% confidence interval for receiver operating characteristic is 0.87 (0.809-0.932).(B) Calibration curve for the diagnostic model. Calibration curve for the borderline lesion ischemia diagnostic model was established by comparing the observed and predicted probability of a positive FFR in patients with borderline lesions of the coronary arteries. The smaller the distance of the scatter from the dashed line, the better the calibration. (C) Decision curve analysis (DCA) for diagnostic

models of ischemia in borderline coronary lesions. None: net benefit when it is assumed that no patients with critical lesions of the coronary arteries would have the outcome (FFR-positive). All: net benefit when all patients with critical coronary lesions are assumed to have an outcome (FFR-positive). model: net benefit of managing critical coronary lesions with a diagnosis of myocardial ischemia based on the diagnostic model estimate. The strategy with the highest net benefit at any given threshold is the preferred strategy.

Figure 4 Normal, FFR-positive and FFR-negative MCG scan and ICA Images.

Figure legend: MCG scan showed no evidence of ischemia or obstructive coronary artery disease, as demonstrated by the lack of significant current deviations within the myocardium and absence of angle shift between the positive red pole and negative blue pole between T wave onset (T-onset) and T wave peak (T-peak) ; (B) The MCG scan of a patient in their 70s showed magnetic field angular deflection , abnormal magnetic field distribution of the positive and multipolarisation of negative poles , suggesting significant myocardial ischemia, and the ECG showed no significant abnormality. The ICA showed two lesions: 60% stenosis of the D1, 50% stenosis of the R-PDA , The FFRs were 0.77 for the R-PDA;(C) MCG scan of a patient in their 60s showed no myocardial ischemia, ECG showed no significant abnormalities, echocardiography showed widening of the ascending aorta and aortic sinus. ICA showed 75% stenosis of the LAD, 60% stenosis of the RCA, FFR value of the LAD was 0.88. MCG= magnetocardiography; FFR= fractional flow reserve ; ICA= invasive coronary angiography; D1= Diagonal branches ; R-PDA : Posterior descending artery ; LAD= Left Anterior descending artery; RCA= right coronary artery.

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Patients with borderline coronary artery lesions enrolled in the study		Selection of parameters and development of the diagnostic model		Diagnostic mode
Patient with angina or 40-90% stenosis on CCTA from June 30 to November 30,2023 N=163		65 OPM-MCG output parameters		Model development
v	Excluded: poor quality of MCG imaging N=4		Excluded: P value of univariable logistic regression analysis >0.1 (15 parameters)	
Patients completed OPM-MCG N=159				
	Excluded: patients with stenosis >90% N=11	LASSO regression model (50 parameters)		v
Patients with ICA show 40-90% of the heaviest stenosis N=148			Excluded: Considering the rationality of the model LASSO screens out redundant variables	Internal validation an calibration curve
	Excluded: Patients who did not complete FFR evaluation prior to PCI	v	(44 parameters)	
	N=7	Multivariate logistic regression analysis		
Patients completed FFR evaluation N=141		(8 parameters)		
	-		Excluded: Construction of a diagnostic model through the backward approach (2) requestors)	

Figure 1. Flowchart of the study design.

Figure legend : CCTA= coronary computed tomography angiography; MCG=magnetocardiography; ICA= invasive coronary angiography; FFR=fractional flow reserve; PCI= percutaneous coronary intervention.

1139x537mm (96 x 96 DPI)





Figure 3 Accuracy and internal validation of the diagnostic model.

Figure legend: (A) ROC curves and 95% confidence intervals. After 500 bootstrap replications, the area under the curve and 95% confidence interval for receiver operating characteristic is 0.87 (0.809-0.932).(B) Calibration curve for the diagnostic model. Calibration curve for the borderline lesion ischemia diagnostic model was established by comparing the observed and predicted probability of a positive FFR in patients with borderline lesions of the coronary arteries. The smaller the distance of the scatter from the dashed line, the better the calibration. (C) Decision curve analysis (DCA) for diagnostic models of ischemia in borderline coronary lesions. None: net benefit when it is assumed that no patients with critical lesions of the coronary arteries would have the outcome (FFR-positive). All: net benefit when all patients with critical coronary lesions are assumed to have an outcome (FFR-positive). model: net benefit of managing critical coronary lesions with a diagnosis of myocardial ischemia based on the diagnostic model estimate. The strategy with the highest net benefit at any given threshold is the preferred strategy.

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Figure 4 Normal, FFR-positive and FFR-negative MCG scan and ICA Images.

Figure legend: MCG scan showed no evidence of ischemia or obstructive coronary artery disease, as demonstrated by the lack of significant current deviations within the myocardium and absence of angle shift between the positive red pole and negative blue pole between T wave onset (T-onset) and T wave peak (T-peak) ; (B) The MCG scan of a patient in their 70s showed magnetic field angular deflection , abnormal magnetic field distribution of the positive and multipolarisation of negative poles , suggesting significant myocardial ischemia, and the ECG showed no significant abnormality. The ICA showed two lesions: 60% stenosis of the D1, 50% stenosis of the R-PDA ,. The FFRs were 0.77 for the R-PDA;(C) MCG scan of a patient in their 60s showed no myocardial ischemia, ECG showed no significant abnormalities, echocardiography showed widening of the ascending aorta and aortic sinus. ICA showed 75% stenosis of the LAD, 60% stenosis of the RCA, FFR value of the LAD was 0.88.

MCG= magnetocardiography; FFR= fractional flow reserve ; ICA= invasive coronary angiography; D1= Diagonal branches ; R-PDA : Posterior descending artery ; LAD= Left Anterior descending artery; RCA= right coronary artery.

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8	Supplementary Material 9 0	
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10	Assessment of myocardial ischemia in borderline coronary artery lesions based on optical pumber magnetometer	
11	magnetocardiography	
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14	Shuwen Yang1#, Lanxin Feng 1#, Zhao Ma1, Huan Zhang1, Yazhe Zhang2, Linqi Liu1, Shu Zhou1, Xin Zhao1, Xingi a Yang1, Mingduo	
15	Zhang1, Min Zhang1, Jiqiang He1, Yanlong Ren1, Yawei Luo1, Feng Xu1, Xiantao Song1*, Chenchen Tu1*, Hong RadZhang2	
16	#These authors contributed equally to this work	
17	Department of Cardiology Rejijing Anzhen Hospital Capital Medical University 100020 Rejijing China	
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CCTA= coronary computed tomography angiography; MCG=magnetocardiography; ICA= invasive coronary angiography; FFR=fractional flow reserve; PCI= percutaneous coronary intervention. Ĉe

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 error (SE). The red dotted line indicates the cross-validation curve. The vertical dashed lines are drawn at the optimal values on the basis of the minimum criteria and 1-SE criteria. Considering the reasonableness of the variables included in this model, with the value of 0.02380779 was chosen. Jraphique de l

Table 1 OPM-MCO Parameters δ Agmax-M δ Agmin-M δ Agsun-M δ Agsum-M δ Dtmax-PN	G Parameters and Definitions Generation and the standard deviation of changes in magnetic field angle at intervals of a certain time twithing TT segment The minimum value of changes in magnetic field angle at intervals of a certain time twithing TT segment The standard deviation of changes in magnetic field angle at intervals of a certain time twithing TT segment
$\frac{\text{Table 1 OPM-MCO}}{\text{Parameters}}$ $\frac{\delta \text{ Ag}_{max}\text{-M}}{\delta \text{ Ag}_{min}\text{-M}}$ $\frac{\delta \text{ Ag}_{std}\text{-M}}{\delta \text{ Ag}_{std}\text{-M}}$ $\frac{\delta \text{ Ag}_{sum}\text{-M}}{\delta \text{ Dt}_{max}\text{-PN}}$	G Parameters and Definitions G Parameters and Definitions Definition G Parameters and Definition The maximum value of changes in magnetic field angle at intervals of a certain time T within T segment The minimum value of changes in magnetic field angle at intervals of a certain time T within T segment The standard deviation of changes in magnetic field angle at intervals of a certain time T within T segment
	G Parameters and Definitions Image: Second Seco
δ Ag _{max} -M δ Ag _{min} -M δ Ag _{std} -M δ Ag _{sum} -M δ Dt _{max} -PN	The maximum value of changes in magnetic field angle at intervals of a certain time τ within TB segment The minimum value of changes in magnetic field angle at intervals of a certain time τ within TB segment The standard deviation of changes in magnetic field angle at intervals of a certain time τ within TT segment
δ Ag _{min} -M δ Ag _{std} -M δ Ag _{sum} -M δ Dt _{max} -PN	The minimum value of changes in magnetic field angle at intervals of a certain time τ within TTS segment The standard deviation of changes in magnetic field angle at intervals of a certain time τ within TTS segment
δ Ag _{std} -M δ Ag _{sum} -M δ Dt _{max} -PN	The standard deviation of changes in magnetic field angle at intervals of a certain time τ within T segment
δ Ag _{sum} -M δ Dt _{max} -PN	
δDt_{max} -PN	The sum of changes in magnetic field angle at intervals of a certain time. T. within TT segments
$O Dl_{max}$ -r IN	The maximum value of changes in magnetic pole distance at intervals of a certain time τ , within 11 segment.
δ Dt DN	The minimum value of changes in magnetic pole distance at intervals of a certain time to within T segment
$\delta Dt DN$	The standard deviation of changes in magnetic pole distance at intervals of a certain time. The standard deviation of changes in magnetic pole distance at intervals of a certain time.
$\delta Dt DN$	The sum of abanges in magnetic pole distance at intervals of a certain time. To within TT segment
$\delta \Delta \alpha = C$	The maximum value of changes in current angle at intervals of a certain time. To within TT segments
$\delta Ag C$	The minimum value of changes in current angle at intervals of a certain time. To within TT setting the
δAg_{min} -C	The standard deviation of changes in current angle at intervals of a certain time τ within TTERES.
δAg_{std} -C	The sum of changes in current angle at intervals of a certain time. To within TT segment
$\delta \mathbf{Ag}_{sum}$ -C	The maximum value of changes in the nocition of the surment on all of intervals of a certain time.
$\circ PS_{max}$ -C	The stendard deviation of changes in the position of the current angle at intervals of a certain time within TT segmen
$\circ PS_{std}$ -C	The sum of changes in the position of the current angle at intervals of a certain time $\frac{1}{2}$ within 11 segme
• PS _{sum} -C	The sum of changes in the position of the current angle at intervals of a certain time t withing I is segment
• Ar _{max} -NP	The maximum value of changes in negative pole point area at intervals of a certain time t wathing I I segment
• Ar _{min} -NP	The minimum value of changes in negative pole point area at intervals of a certain time t withing I segment
٥ Ar _{std} -NP	The standard deviation of changes in negative pole point area at intervals of a certain time $\tau = \frac{1}{2}$ within TT segment
٥ Ar _{sum} -NP	The sum of changes in negative pole point area at intervals of a certain time τ within TT segment
٥ Ar _{bp} -NP	The change in negative pole point area between T-begin and T-peak
Ar _{max} -NP	The maximum value of the negative pole point area at intervals of a certain time τ within T \mathbf{P} segment
Ar _{min} -NP	The minimum value of the negative pole point area at intervals of a certain time τ within THese section that the section of the negative pole point area at intervals of a certain time τ within THese sections are a section of the negative pole point area at intervals of a certain time τ within THese sections are a section of the negative pole point area at intervals of a certain time τ within THEse sections are a section of the negative pole point area at intervals of a certain time τ within THEse sections are a section of the negative pole point area at intervals of a certain time τ within THEse sections are a section of the negative pole point area at intervals of a certain time τ within THEse sections are at the negative pole point area at intervals of a certain time τ within THEse sections are at the negative pole point area at intervals of a certain time τ within THEse sections are at the negative pole point area at the negative pole pole pole point area at the negative pole pole pole pole pole pole pole pol
δ Ps _{max} -NP	The maximum value of changes in the position of the negative pole point at intervals of a central segment τ with segment
δPs_{std} -NP	The standard deviation of changes in the negative of the positive pole point at intervals of a central time τ with segment
δ Ps _{sum} -NP	The sum of changes in the position of the negative pole point at intervals of a certain time τ with $\frac{1}{2}$ m TT segment
δ Ar _{max} -N	The maximum value of changes in negative pole area at intervals of a certain time τ within TT suggement

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Parameters	Definition
δ Ag _{max} -M	The maximum value of changes in magnetic field angle at intervals of a certain time τ with $\frac{1}{2}$ T is segment
δ Ar _{min} -N	The minimum value of changes in negative pole area at intervals of a certain time τ within \mathbf{E} s segment
$\delta \operatorname{Ar}_{std}-N$	The standard deviation of changes in negative pole area at intervals of a certain time τ with \mathbf{e} T respectively.
δ Ar _{sum} -N	The sum of changes in negative pole area at intervals of a certain time τ within TT segment $\frac{1}{2}$
δ Ar _{bp} -N	The change in nagative pole area between T-begin and T-peak
Ar _{max} -N	The maximum value of the negative pole area at intervals of a certain time τ within TT segregized to
Ar _{min} -N	The minimum value of the negative pole area at intervals of a certain time τ within TT segnet \mathbf{x}
δ ArRto _{max} -PN	The maximum value of changes in the ratio of positive and negative pole area at intervals of \vec{a} tain time τ within TT segment
δ ArRto _{min} -PN	The minimum value of changes in the ratio of positive and negative pole area at intervals of \vec{a} tain time τ within TT segment
δ ArRto _{std} -PN	The standard deviation of changes in the ratio of positive and negative pole area at intervals of $\mathbf{p}_{\mathbf{x}}$ represent within TT segment
δ ArRto _{sum} -PN	The sum of changes in the ratio of positive and negative pole area at intervals of a certain time $\sum \tau$ within TT segment
δ Ar _{max} -PP	The maximum value of changes in positive pole point area at intervals of a certain time v within T segment
δ Ar _{min} -PP	The minimum value of changes in positive pole point area at intervals of a certain time τ within T segment
δ Ar _{std} -PP	The standard deviation of changes in positive pole point area at intervals of a certain time τ with TT segment
δ Ar _{sum} -PP	The sum of changes in positive pole point area at intervals of a certain time τ within TT segments
δ Ar _{bp} -PP	The change in positive pole point area between T-begin and T-peak
Ar _{max} -PP	The maximum value of the positive pole point area at intervals of a certain time τ within TT segment
Ar _{min} -PP	The minimum value of the positive pole point area at intervals of a certain time τ within TT $\frac{2}{3}$ eg and $\frac{1}{3}$ eg
δ Ps _{max} -PP	The maximum value of changes in the position of the positive pole point at intervals of \vec{a}_{ce} certain time τ within TT segment
$\delta \mathbf{P} \mathbf{S}_{\text{std}} \textbf{-} \mathbf{P} \mathbf{P}$	The standard deviation of changes in the position of the positive pole point at intervals of a $rac{s}{r}$ at time τ within TT segment
δ Ps _{sum} -PP	The sum of changes in the position of the positive pole point at intervals of a certain time τ with \vec{a} TT segment
δ Ar _{max} -P	The maximum value of changes in positive pole area at intervals of a certain time τ within TT segment
δ Ar _{min} -P	The minimum value of changes in positive pole area at intervals of a certain time τ within TT s methods from the second secon
δAr_{std} -P	The standard deviation of changes in positive pole area at intervals of a certain time τ within Tresegment
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	Parameters	Definition
	δ Ag _{max} -M	The maximum value of changes in magnetic field angle at intervals of a certain time τ with $\frac{2}{3}$ T is segment
	δ Ar _{sum} -P	The sum of changes in positive pole area at intervals of a certain time τ within TT segment $\frac{1}{2}$
	δ Ar _{bp} -P	The change in positive pole area between T-begin and T-peak
	Ar _{ma} x-P	The maximum value of the positive pole area at intervals of a certain time τ within TT segnerated by
	Ar _{min} -P	The minimum value of the positive pole area at intervals of a certain time τ within TT segmer \vec{a}
	MAg _{max} -TT	The maximum magnetic field angle at intervals of a certain time τ within TT segment
	CAg _{max} -TT	The maximum current angle at intervals of a certain time τ within TT segment
	MAg _{min} -TT	The minimum magnetic field angle at intervals of a certain time τ within TT segment
	CAg _{min} -TT	The minimum current angle at intervals of a certain time τ within TT segment
	MAg-Rp	The magnetic field angle of the R-peak
	RtoAm-R _p T _p N	The ratio of magnetic field amplitude at R-peak and the negative amplitude at T-peak
	RtoAm-R _p T _p P	The ratio o magnetic field amplitude at R-peak and the positive amplitude at T-peak
	RtoAm-R _p T _p	The ratio of magnetic field amplitudes at R-peak and T-peak
	MAg-RpTp	The magnetic field angle between R-peak and T-peak
	MAg-Tp	The magnetic field angle of the T-peak
	CAg _{max} -Tp	The maximum current angle at T-peak
	RtoAm-Tp	The ratio of positive to negative magnetic field amplitude at T-peak
	TT	The interval from the beginning of the T-wave to its peak within the cardiac cycle
Ē	Dt = Distance, Ps	$s = Position$, Ag = Angle, Am = Magnitude, Ar = Area, Rto = Ratio, P = Positive, Positive \mathbf{E} PP, Negative = N, \mathbf{E}
T	T = TT segment	
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ble 2 OPM-MC	G parameters of the Participan	t and univariable logistic regr	ession model	-08643	
Parameters	ALL	FFR-Positive	FFR-Negative	Hazard Ratio	P value
	0 (2 (0 44 1 10)	N=08		<u>ਰ੍ਹੇ (%)%CI)</u>	
• Ag _{max} -M	0.62 (0.44,1.19)	0.//(0.4/,5./6)	0.54 (0.43,0.72)		0.002
• Ag _{min} -M	-0.34 (-0.57,-0.18)	-0.42 (-0.82,-0.28)	-0.26 (-0.42,-0.14)		0.001
• Ag _{std} -M	0.16 (0.11,0.68)	0.28 (0.14,2.06)	0.14 (0.10,0.20)		< 0.00
• Ag _{sum} -M	10.6 (6.18,26.2)	20.2 (9.88,45.5)	8.28 (4.55,11.8)		< 0.00
• Dt _{max} -PN	2.69 (1.97,4.12)	3.51 (2.16,12.9)	2.22 (1.89,3.16)		< 0.00
٥ Dt _{min} -PN	-2.20 (-3.27,-1.76)	-2.38 (-4.70,-1.91)	-2.00 (-2.80,-1.63)	0,000,000,000,1.00)	0.003
o Dt _{std} -PN	0.74 (0.55,1.18)	0.82 (0.63,3.45)	0.63 (0.52,0.89)		0.001
δ Dt _{sum} -PN	46.6 (29.1,80.7)	66.6 (42.0,110)	33.3 (25.7,48.6)		< 0.00
δ Ag _{max} -C	1.70 (1.21,4.83)	1.79 (1.27,9.10)	1.52 (1.16,2.98)		0.016
δ Ag _{min} -C	-1.24 (-3.81,0.00)	-1.70 (-8.89,-1.01)	-0.91 (-1.75,0.00)	0,97,1.00)	< 0.00
δAg_{std} -C	0.54 (0.36,1.32)	0.80 (0.37,3.16)	0.45 (0.34,0.70)	1 2 G .01,1.23)	0.003
δ Ag _{sum} -C	15.6 (9.64,38.6)	29.8 (13.5,71.6)	11.9 (7.79,17.5)		< 0.00
δ Ps _{max} -C	33.0 (1.00,48.8)	33.0 (1.41,125)	31.0 (1.00,34.0)	1501 8 .00,1.01)	0.008
δ Ps _{std} -C	3.35 (0.24,6.16)	3.57 (0.29,11.7)	3.20 (0.24,4.86)	01,1.13) و	0.016
δ Ps _{sum} -C	39.1 (6.00,86.1)	74.4 (8.31,161)	33.4 (4.00,66.0)	1 9 01 8 1.00,1.01)	< 0.00
δ Ar _{max} -NP	136 (74.0,220)	182 (102,314)	105 (59.0,180)		< 0.00
δ Ar _{min} -NP	-84.00 (-173.00,-54.00)	-99.00 (-187.50,-62.75)	-68.00 (-148.00,-46.00)		0.009
$\delta \operatorname{Ar}_{std}$ -NP	29.6 (20.0,56.7)	31.7 (23.4,70.1)	25.7 (17.1,41.4)		0.004
δ Ar _{sum} -NP	2469 (1443,4286)	3369 (2230,5728)	1672 (1277,2987)		< 0.00
δ Ar _{bp} -NP	944 (18.0,2830)	1168 (152,3066)	626 (-46.00,2383)	1 9 00 8 .00,1.00)	0.238
Ar _{max} -NP	3873 (3001,5765)	4269 (3260,6056)	3828 (2894,5406)	1.00 [1.00,1.00]	0.160
Ar _{min} -NP	2426 (1639,3326)	2094 (1436,3245)	2614 (2065,3360)	1.00 2.00,1.00)	0.036
δ Ps _{max} -NP	2.83 (2.24,4.12)	3.00 (2.24,5.28)	2.24 (2.00,3.00)	1.01 8 .00,1.01)	0.005
δPs_{std} -NP	0.70 (0.57,1.00)	0.81 (0.65,1.20)	0.66 (0.51,0.85)	1.04 🛱 .98,1.11)	0.005
δPs_{sum} -NP	41.7 (22.2,79.9)	59.8 (39.8,104)	26.4 (20.1,51.1)	1.01 (01,1.02)	< 0.00
δ Ar _{max} -N	435 (243,750)	539 (269,990)	404 (221,526)	1.00 ឆ្នាំ.00,1.00)	0.017

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2 3 4 5	Parameters	ALL N=141	FFR-Positive N=68	FFR-Negative N=73	<u>9</u> 	P value
6 – 7	δ Ar _{min} -N	-170.00 (-369.00,-25.00)	-267.00 (-565.25,-108.75)	-79.00 (-224.00,-15.00)	1,00,1.00)	< 0.001
8	δ Ar _{std} -N	125 (80.2,225)	160 (90.5,273)	114 (74.6,158)	1,00 g .00,1.01)	0.004
9	δ Ar _{sum} -N	12585 (7372,23204)	19058 (10208,29054)	9520 (6202,15009)	1.00,1.00)	< 0.001
10	δ Ar _{hn} -N	10445 (1116,25689)	11528 (588,28595)	8107 (2900,16796)		0.840
11	Ar _{max} -N	53635 (43655,65410)	56546 (44597,77766)	51431 (38201,58878)		0.032
13	Ar _{min} -N	40985 (26175,53701)	39744 (24308,59155)	40985 (29379,49923)		0.644
14 15 16	δ ArRto _{max} -PN	0.01 (0.00,0.02)	0.01 (0.00,0.03)	0.00 (0.00,0.01)	(5.89(1)) (5.89(< 0.001
17	δ ArRto _{min} -PN	-0.02 (-0.05,-0.01)	-0.02 (-0.07,-0.01)	-0.02 (-0.04,-0.01)	0 .00,0.13)	0.134
18 19 20	δ ArRto _{std} -PN	0.01 (0.00,0.02)	0.01 (0.00,0.02)	0.01 (0.00,0.01)	المعادمة (1.75 المعادمة من 1.5 من 1	0.114
21	δ ArRto _{sum} -PN	0.63 (0.32,1.72)	0.85 (0.39,2.36)	0.58 (0.29,0.88)	154 (15,2.06)	0.014
22	δ Ar _{max} -PP	195 (126,404)	281 (141,704)	• 153 (111,286)	1 200 8 .00,1.00)	0.001
23	δ Ar _{min} -PP	-171.00 (-295.00,-106.00)	-196.00 (-563.75,-109.50)	-153.00 (-226.00,-104.00)	1 1 00,1.00)	0.006
25	δ Ar _{std} -PP	54.3 (33.7,124)	77.3 (35.5,167)	43.7 (32.1,79.7)	jā01 d. 00,1.01)	0.007
26	δ Ar _{sum} -PP	4689 (2685,8783)	6608 (3410,14024)	3487 (2556,5786)	1200 1.00,1.00)	< 0.001
27	δ Ar _{bp} -PP	1058 (-869.00,5166)	1360 (-872.25,5756)	737 (-869.00,4601)	1 🛱 00 🛱 .00,1.00)	0.872
28 29	Ar _{max} -PP	8775 (6335,13548)	9178 (6485,14820)	8775 (6335,12776)	1 20 8 .00,1.00)	0.386
30	Ar _{min} -PP	5151 (2774,7571)	4626 (2618,6928)	5754 (3719,8258)	າສັ້ງ0 ຊີ້ .00,1.00)	0.054
31	δ Ps _{max} -PP	3.16 (2.24,5.00)	3.61 (3.00,100)	3.00 (2.24,3.61)	1 201 (2.00,1.02)	< 0.001
32	δ Ps _{std} -PP	0.82 (0.60,1.15)	0.98 (0.66,8.50)	0.75 (0.57,0.90)	1012 (1.04,1.20)	< 0.001
34	δ Ps _{sum} -PP	40.4 (23.1,88.6)	73.8 (29.9,195)	32.8 (21.7,54.2)	1.01,1.02)	< 0.001
35	δ Ar _{max} -P	244 (90.0,430)	312 (150,692)	172 (70.0,362)	1.00	0.001
36	δ Ar _{min} -P	-348.00 (-592.00,-203.00)	-381.00 (-812.00,-188.75)	-311.00 (-497.00,-211.00)	1.00 (2.00,1.00)	0.150
38	δ Ar _{std} -P	120 (80.2,203)	135 (82.3,267)	109 (75.7,159)	1.00 (1.00,1.00)	0.105
39	δ Ar _{sum} -P	11899 (6525,19157)	15787 (7938,28576)	9566 (5985,15629)	1.00 8 .00,1.00)	0.002
40 41	δ Ar _{bp} -P	-3600.00	-1456.00 (-14861.75,3900)	-4007.00	1.00	0.533
42 43 44					shique	
45		For peer re	view only - http://bmjopen.bmj.	com/site/about/guidelines.xhti	ml de	

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Parameters $(-Ar_{max}-P)$ $Ar_{min}-P$ $Ar_{min}-P$ $Ag_{max}-TT$ $-62.$ $CAg_{max}-TT$ $-62.$ $CAg_{min}-TT$ $-62.$ $CAg_{min}-TT$ $-62.$ $CAg_mr_p T_p$ $-62.$ $MAg-RpTp$ $-62.$ $MAg-RpTp$ $-62.$ $MAg-RpTp$ $-64.$ $CAg_{max}-Tp$ $-64.$ $CAg_{max}-Tp$				2 W	
$\begin{array}{c}(\cdot \\ Ar_{max}-P \\ Ar_{min}-P \\ 8982 \\ MAg_{max}-TT \\ -62. \\ CAg_{max}-TT \\ -62. \\ CAg_{max}-TT \\ -62. \\ CAg_{max}-TT \\ -62. \\ CAg_{max}-TT \\ -70. \\ CAg_{max}-TT \\ -70. \\ CAg_{max}-TT \\ -70. \\ -62. \\ CAg_{max}-Tp \\ -62. \\ CAg_{max}-Tp \\ -64. \\ CAg_{max}-Tp \\ $	ALL	FFR-Positive	FFR-Negative	opyright, Hazard Ratio	P
$\begin{array}{c}(\cdot \\ Ar_{max}-P \\ Ar_{min}-P \\ 898. \\ MAg_{max}-TT \\ -62. \\ CAg_{max}-TT \\ -62. \\ CAg_{max}-TT \\ -62. \\ CAg_{max}-TT \\ -61. \\ Rto_{max}-TT \\ -70. \\ CAg_{min}-TT \\ -70. \\ CAg_{min}-TT \\ -70. \\ CAg_{min}-TT \\ -70. \\ -62. \\ CAg_{max}-Tp \\ -64. \\ CAg_{max}-Tp \\ $	N=141	N=68	N=73	<u> </u>	
$Ar_{max}$ -P $Ar_{min}$ -P       898. $MAg_{max}$ -TT       -62. $CAg_{max}$ -TT       -62. $CAg_{max}$ -TT       -62. $CAg_{max}$ -TT       -62. $MAg_{max}$ -TT       -62. $MAg_{max}$ -TT       -62. $MAg_{max}$ -TT       -62. $MAg_{max}$ -TT       -62. $MAg_{min}$ -TT       -70. $CAg_{min}$ -TT       -70. $MAg$ -Rp       -61. $MAg$ -Rp       -61. $RtoAm$ - $R_pT_pN$ 60. $RtoAm$ - $R_pT_pP$ -70. $MAg$ -RpTp       -70. $MAg$ -RpTp       -64. $CAg_{max}$ -Tp       -64. $CAg_{max}$ -Tp       -64. $CAg_{max}$ -Tp       -64.	-12686.00,2509)		(-10962.00,1528)	1 26 19 fo	
Ar min-P898MAg max-TT-62CAg max-TT-62CAg 	97097 (33699)	95392 (37311)	98685 (30122)	1700 <b>Q</b> .00,1.00)	0
MAgmax-TT-62. $CAg_{max}$ -TT4 $MAg_{min}$ -TT-70. $CAg_{min}$ -TT-70. $CAg_{min}$ -TT-70. $CAg_{min}$ -TT-70. $MAg$ -Rp-61.RtoAm-RpTpN60.RtoAm-RpTpP-70.RtoAm-RpTp-70.MAg-RpTp-0.MAg-Tp-64.CAg_max-Tp-4.	22 (63201,104875)	83948 (55748,104204)	92433 (68813,105383)	1809; el.00,1.00)	0
CAg max-TT4MAg min-TT-70.CAg min-TT-70.CAg min-TT-70.CAg min-TT-61.RtoAm-R pTp-61.RtoAm-R pTp-61.RtoAm-R pTp-61.RtoAm-R pTp-61.RtoAm-R pTp-61.MAg-RpTp-61.MAg-RpTp-64.CAg max-Tp-64.	.32 (-70.64,-34.61)	-48.00 (-66.89,15.5)	-67.39 (-72.03,-53.13)		<(
MAgmin-TT-70.CAgmin-TT $\therefore$ MAg-Rp-61.RtoAm-RpTpN $\bigcirc$ RtoAm-RpTpP $\therefore$ RtoAm-RpTp $\bigcirc$ MAg-RpTp-0MAg-Tp-64.CAgmax-Tp $\bigcirc$	45.0 (33.3,71.0)	58.2 (39.2,118)	43.1 (32.0,51.1)		<(
CAgmin-TT $\therefore$ MAg-Rp-61.RtoAm-RpTpN6RtoAm-RpTpP $\therefore$ RtoAm-RpTp $\therefore$ MAg-RpTp-0MAg-Tp-64.CAgmax-Tp4	.76 (-76.85,-56.92)	-68.28 (-75.62,-41.24)	-71.98 (-77.61,-64.94)		0
MAg-Rp-61.RtoAm- $R_pT_pN$ 6RtoAm- $R_pT_pP$ 7RtoAm- $R_pT_p$ 7MAg-RpTp-0MAg-Tp-64.CAg _{max} -Tp2	32.8 (5.36,45.9)	34.7 (-10.80,63.8)	32.0 (12.3,44.0)		0
RtoAm- $R_pT_pN$ ()RtoAm- $R_pT_pP$ ()RtoAm- $R_pT_p$ ()MAg- $RpTp$ -0MAg- $Tp$ -64.CAg _{max} - $Tp$ ()	.41 (-71.15,-42.88)	-53.44 (-70.66,-38.24)	-65.92 (-71.78,-50.54)	1309 <u>6</u> .00,1.03)	0
RtoAm- $R_pT_pP$ $2$ RtoAm- $R_pT_p$ $3$ MAg- $RpTp$ -0MAg- $Tp$ -64CAg _{max} - $Tp$ $4$	5.49 (4.32,9.57)	7.35 (4.92,10.4)	5.68 (3.71,8.14)	1905 <u>(</u> .00,1.12)	0
RtoAm- $R_pT_p$ $C$ MAg- $RpTp$ -0MAg- $Tp$ -64CAg _{max} - $Tp$ -64	7.97 (5.88,12.0)	8.66 (6.03,12.9)	7.69 (5.56,11.1)		0
MAg-RpTp -0 MAg-Tp -64. CAg _{max} -Tp 2	3.64 (2.38,4.70)	4.13 (3.08,5.01)	3.28 (2.36,4.50)	1522 (1.04,1.43)	0
MAg-Tp -64. CAg _{max} -Tp 2	0.67 (-24.77,19.5)	3.61 (-25.62,33.8)	-2.72 (-22.99,13.2)	1 <b>→</b> 00 <b>(</b> .00,1.01)	0
CAg _{max} -Tp 4	.66 (-71.34,-45.44)	-55.82 (-70.28,-12.79)	-67.91 (-72.69,-53.13)	1 2 6 .01,1.03)	0
	43.1 (29.4,52.0)	45.0 (27.6,74.7)	42.2 (30.7,46.9)	191 (1.00,1.02)	0
RtoAm-Ip (	0.76 (0.57,1.08)	0.81 (0.52,1.22)	0.75 (0.57,0.98)	<b>1</b> ,52 <b>1</b> ,93,2.48)	0
Dt = Distance. Ps = Posi ⁺	tion. Ag = Angle. An	n = Magnitude, Ar = Area, F	$R_{to} = R_{atio}, P = Positive, P$	itive Pole PP. Negati	ve = N
Negative Pole, M = Magn	etic Field, C = Current	t, max = Maximum, min = Mi	nimum, sum=Sum of all, std =	Standard deviation, $\delta =$	Chang
TT= TT segment	,	, , ,		ilar ý	U
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Page 37 of 35				BMJ Open		6/bmjopen-20; cted by copyri	
2 3 4 5	Table 3 Diagnostic mod	lel for assessment of my	ocardial isch	emia in borderline co	ronary artery lesions	24-086433 ight, inclu	
6		Daramatara		Diag	gnostic model	on ding	
7		Farameters	В	OR	95%CI	<b>B</b> value	
8 9		MAgmax-TT	0.011	1.011	(1.000-1.021)	\$7.002	
10		CAgmax-TT	0.008	1.008	(0.998-1.018)		
11		δAgsum-C	0.008	1.009	(1.000-1.019)		
12		δPssum-PP	0.007	1.007	(1.001-1.013)		
13 14		δArsum-N	0.001	1.001	(1.000-1.001)	5 5 D D D	
15		RtoArmax-PN	17.324	33409.498	(0.694-50738)		
16	Ps = Position Ag = Ar	ngle $Ar = Area Rto =$	Ratio $P = P$	ositive Positive Pole	e = PP Negative = N M =		= Current max =
19         20         21         22         23         24         25         26         27         28         29         30         31         32         33         34         35         36         37         38         39         40         41         42         43         44						m http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique BES) . mining, Al training, and similar technologies.	
44		For peer r	eview only - ht	ttp://bmjopen.bmj.com	n/site/about/guidelines.xhtm	l de l	

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# Assessment of myocardial ischemia in borderline coronary artery lesions based on optical pumped magnetometer magnetocardiography

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1	Assessment of myocardial ischemia in borderline coronary artery lesions based on optical pumped
2	magnetometer magnetocardiography
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21	
	1

23	Abstract
24	Aims: Despite clinical guideline recommendations for its use, the uptake of fractional flow reserve
25	(FFR) in borderline coronary artery lesions remains low. As a noninvasive and safe test for myocardial
26	ischemia, the validity of optical pumped magnetometer magnetocardiography (OPM-MCG) versus FFR
27	has not been fully established. Methods and Results: A total of 141 stable patients with borderline
28	coronary artery lesions were prospectively enrolled from June 30 to November 30, 2023. All of them
29	underwent sequential OPM-MCG before coronary angiography (CAG) and FFR. 6 parameters were
30	included in the final diagnostic model: MAg _{max} -TT, CAg _{max} -TT, $\delta$ Ag _{sum} -C, $\delta$ Ps _{sum} -PP, $\delta$ Ar _{sum} -N and
31	RtoAr _{max} -PN. 500 bootstrap replications showed that the area under the receiver operating characteristic
32	curve 95% confidence interval of the diagnostic model was 0.87 (0.809-0.932), with sensitivity of 76.5%,
33	specificity of 91.8%, positive predictive value of 89.7%, negative predictive value of 80.7%. 1000
34	bootstrap replications showed that the model was well-calibrated. Decision curve analysis showed a net
35	benefit from the predictive model when the threshold probability of an ischemic patient was greater than
36	12%, suggesting the potential utility of the model in the real world. <b>Conclusion:</b> A nomogram based on
37	6 OPM-MCG parameters was built to assess myocardial ischemia in borderline coronary artery lesions
38	and can reduce unnecessary CAG.

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# 40 Strengths and limitations of this study

1) This study is the first to demonstrate the importance of OPM-MCG in diagnosing myocardialischemia in patients with borderline coronary lesions.

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43 2) It creates a diagnostic model and nomogram for clinical use.

44 3) The conclusions of this study require further validation through multicenter studies.

**Keywords:** borderline coronary artery lesions; optical pumped magnetometer magnetocardiography;

fractional flow reserve; myocardial ischemia

49 Introduction

Borderline coronary lesions exhibit ranging from 40% to 90% as seen in invasive coronary angiography (CAG). The FAME study ^[1] found that over 80% of lesions fell into this category, with only 35% of stenoses between 50-70% being hemodynamically significant. Predicting relevance was most accurate when estimating coronary artery diameter over 90%. Therefore, fractional flow reserve (FFR) guided intervention in patients with borderline coronary artery lesions (40-90% stenosis) has become a recommended treatment strategy in the 2018 ESC Interventional Guidelines ^[2]. The 2021 ACC/AHA/SCAI Guidelines for Coronary Artery Revascularization ^[3] also have clear recommendations for borderline lesions: FFR and instantaneous wave-free ratio (iFR) are used to assess the need for percutaneous coronary intervention (PCI) in patients without evidence of ischemia but with angina and other equivalent symptoms (Class I); PCI is not recommended for stable patients with FFR >0.8 or iFR >0.89 (Class III). However, its widespread adoption in coronary catheter laboratories is hindered by its time-consuming nature, consumption of resources, and potential adverse effects associated with adenosine application. 

Optical pumped magnetometer magnetocardiography (OPM-MCG) measures tiny magnetic fields

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 $(10^{-15} \text{ Tesla})$  from the heart using atomic magnetometer technology, without radiation. It's quick, contactless, and suitable for diverse populations. Clinical studies have shown that MCG is better than electrocardiogram (ECG) at detecting early myocardial ischemia [4,5,6,7] and has similar diagnostic effectiveness as SPECT for coronary artery disease (CAD)^[8,9]. MCG is precise in diagnosing non-STsegment elevation myocardial infarction, even in individuals who do not exhibit typical angina. ^[10,11]. However, the parameters and cut-off values of OPM-MCG that indicate myocardial ischemia are presently undefined in borderline coronary artery lesion. 

Hence, this study aims to investigate the accuracy of OPM-MCG in diagnosing myocardial ischemia in patients with borderline coronary lesions, with invasive FFR examination serving as the e ele reference standard.

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Method 

#### **Study population**

This study was a prospective, single-center, observational, cohort study which was reviewed by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University, and registered with the China Clinical Trial Registry (ChiCTR2300072382). All participants signed an informed consent. The methods described in this article follow the STARD 2015 guidelines. 

Participants aged 18-80 with typical angina symptoms (CCS class II or higher) or 40-90% stenosis on CCTA were scheduled for hospitalization for CAG. Exclusion criteria included: 1) Coronary artery stenosis outside of 40%-90% range on CAG; 2) Acute myocardial infarction; 3) Previous myocardial infarction; 4) Complex arrhythmias; 5) Bundle-branch block; 6) Pacemakers, metallic implants in trunk; 

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85 7) Claustrophobia.

This study was based on a prospective cohort design, the sample size of which was calculated by PASS 2021 software using the area under the ROC curve. The significance level ( $\alpha$ ) was 0.025 and the degree of certainty (1- $\beta$ ) was 0.90, combining the results of the literature review of related studies as well as the statistics of the small sample in the previous period, and calculating according to the FFRpositive (ischemic)/FFR-negative (non-ischemic) =2:3. The sample size was calculated as 138.

A total of 163 patients from June 30th to November 30th, 2023 were consecutively enrolled, and 22 patients were excluded, of which 11 patients with stenosis >90%, 7 patients underwent direct PCI without FFR testing, and 4 patients with poor quality MCG imaging, and Finally 141 patients with borderline coronary lesions underwent MCG and FFR sequentially (Figure 1). In this study, the cardiologists were not aware of the MCG results at the time of the FFR examination, and the MCG parameters were determined before the FFR examination (Supplementary Figure 1-Graphical Abstract).

# CAG and FFR procedures

99 CAG and FFR measurements were performed on the vessels according to the 2021 100 ACC/AHA/SCAI Guidelines for Coronary Artery Revascularization and Expert consensus on the 101 clinical pathway for FFR measurement in China. After administration of nitroglycerin, a pressure 102 monitoring guidewire was advanced through the stenosis. Hyperemia was attained by administration of 103 intravenous adenosine (140µg/kg/min). The FFR pressure wire was positioned a minimum of 20 mm 104 distal to the stenosis in vessel segments  $\geq$ 2 mm. The presence of an FFR  $\leq$ 0.80 was considered a positive 105 indicator of functional ischemia in patients and was defined as the FFR-positive group.

1		
2 3		
4	106	
5		
6 7	107	MCG imaging
8 9 10	108	The MCG recordings were conducted using a 36-channel OPM-MCG system (Miracle MCG),
11 12 13	109	featuring OPM sensors sourced from Beijing X-Mag Technologies Limited's mature commercial
14 15 16	110	product. The OPM sensor is based on spin-exchange relaxation free (SERF) technology, with alkali
17 18	111	metal atoms as the core sensitive element. The OPM sensor has a sensitivity below 30 fT/Hz $^{1/2}$ , a
19 20 21	112	recording bandwidth of 1 Hz to 40 Hz, a sampling frequency of 200 Hz, and a noise baseline with not
22 23 24	113	higher than 15 fT. The OPM-MCG residual magnetic field is kept below 1.5 nT, and the data acquisition
24 25 26	114	mode is analog signal acquisition (Supplementary Figure 2). Each subject had a 90-second continuous
27 28 29	115	recording at 36 locations (6×6 grid) above the chest using an arrayed sensor grid.
30 31 32	116	
32 33 34	117	MCG Signal Analysis and Statistical Analysis
35 36 37	118	After MCG data acquisition, the software automatically post-processes the signals to generate
38 39	119	magnetic field and current density maps and output 65 parameters (Supplementary Table 1). The 65
40 41 42	120	parameters we output characterize the stability of the current dipole in the TT segment (the position
43 44	121	from one-third of the T max amplitude (T onset) to T max (T peak)) according to the previous studies
45 46 47	122	of Park et al. and Pena et al. Once OPM-MCG data collection is complete, the software automatically
48 49 50	123	generates precise magnetic field and current density maps and outputs their parameters (see
51 52	124	supplementary material for post-processing steps).
53 54 55	125	Data analysis was performed with SPSS 26.0 and R 4.3.2 (http://www.R-project.org/). Counting
56 57 58	126	data were presented as numbers and percentages, while normally distributed measurement data were
58 59 60		v

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shown as mean  $\pm$  standard deviation. Continuous variables that were not normally distributed were presented using median and quartile values. Statistical significance was determined for all analyses with a P-value less than 0.05. Based on this cohort and the principle of LEAST 10 events per variable (10 EPV), we considered the rationality of the parameters included in the diagnostic model and evaluated the number of parameters. The predictive variables were selected from 65 preselected potential candidates and included in the model by univariate logistic regression, LASSO regression, and multivariate logistic regression with the backward method. The stability of the model was determined by cross-validation. The model's predictive performance was assessed using the enhanced bootstrap method and clinical benefit was evaluated using decision curve analysis. The MCG-FFR nomogram was used to report scores for assessing myocardial ischemia with OPM-MCG parameters. **Patient and Public Involvement** Patients make more people aware of the clinical use of the OPM-MCG and how it is examined by sharing news and information about clinical studies with others. Result **Clinical characteristics** The study included 141 patients, mostly male (77.3%) with an average age of  $60.64 \pm 9.70$  years. After MCG scans, all patients underwent CAG and FFR examination, with 48.2% having positive FFR (FFR  $\leq 0.8$ ). A total of 157 vessels were examined, with 47.1% having FFR  $\leq 0.8$ . Interval between MCG and FFR less than 30 days, median 2 days. Most patients had FFR measurements primarily done 

on the LAD. See Supplementary Table 2 for patient clinical characteristics. 

#### Selection of parameters and development of the diagnostic model

50 variables that were statistically significant (P < 0.1) in univariable logistic regression were included in the LASSO regression (Supplementary Table 3 and Supplementary Figure 3), and 8 variables were selected based on the reasonableness of the parameters selected to reduce the model overfitting and covariance through LASSO regression. By using the backward approach, 6 parameters were included in the final diagnostic model: MAg_{max}-TT, CAg_{max}-TT, δAg_{sum}-C, δPs_{sum}-PP, δAr_{sum}-N and RtoAr_{max}-PN (Table 1, Figure 2). The model area under the receiver operating characteristic curve (AUC) obtained from multivariate logistic regression analysis was 0.87, with sensitivity of 76.5%, specificity of 91.8%, positive predictive value of 89.7%, negative predictive value of 80.7%. The nomogram (Figure 3) provides a graphical overview of the diagnostic model using multivariate logistic regression analysis (Supplementary Table 4).

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#### Internal validation and net benefit of the model

The model performance for the diagnosis of myocardial ischemia in borderline coronary artery lesions of the OPM-MCG was evaluated by bootstrap replications.500 bootstrap replications showed that the model AUC and a 95% confidence interval (CI) of 0.87 (0.809-0.932) (Figure 4). 1000 bootstrap replications showed that the model was well-calibrated. The mean absolute error was 0.032 (Figure 4). The decision curve analysis (DCA) for the diagnostic model showed that if the threshold probability of patients is greater than 12% (Figure 4), screening strategies based on the OPM-MCG diagnostic model 

resulted in superior net benefit than screen-none or screen-all strategies.

6 7 0	170	
8 9 10	171	Discussion
11 12 13	172	CAD is presently characterized by an epicardial vascular lesion with a stenosis exceeding 50% in
14 15	173	the CAG. Frequently, this description acts as a reference for heart muscle revascularization. Moreover,
16 17 18	174	FFR can be used to evaluate the existence of myocardial ischemia, with a threshold of 0.8. However, as
19 20	175	illustrated in the Figure 2, the coronary stenosis identified in CAG may not precisely align with the
21 22 23	176	invasive FFR results. This observation is in line with the conclusions drawn in the 2019 ESC Guidelines
24 25 26	177	for Chronic Coronary Syndromes ^[12,13] , emphasizing that the accuracy of determining CAD solely based
27 28	178	on angiographic stenosis was as low as 64% when compared to flow reserve fraction. The positive
29 30 31	179	mismatch rate, where lesions with less than 50% stenosis may demonstrate an FFR $\leq 0.8$ , was 19%,
32 33	180	while the negative mismatch rate, where lesions with over 50% stenosis may result in an FFR value $>$
34 35 36	181	0.8, reached up to one-third. Numerous studies ^[14,15] have consistently demonstrated that FFR-guided
37 38 20	182	stenting leads to superior immediate outcomes and long-term prognosis. Therefore, FFR carries a Class
39 40 41	183	1a recommendation for guiding revascularization in angiographically borderline coronary stenoses in
42 43 44	184	patients with stable angina. The feasibility of diagnosing myocardial ischemia in patients with borderline
45 46	185	lesions using OPM-MCG was shown in our study, when compared to invasive FFR. The collective
47 48 49	186	diagnostic potential of MCG parameters in detecting myocardial ischemia in borderline coronary artery
50 51 52	187	lesions resulted in an AUC of 0.87 (95% CI 0.809 to 0.932). Due to factors such as time consumption,
52 53 54	188	costs, patient-related discomfort, contraindications, and a lack of reimbursement, the current rate of FFR
55 56 57 58	189	utilization in catheterization laboratories in China is less than 6% ^[3] . OPM-MCG allows ischemia 9
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assessment in patients with borderline coronary lesions prior to CAG and has a good concordance with invasive FFR. 

In comparing our MCG results with those reported by Park JW et al. ^[16], it is clear that FFR, serving as the reference standard, evaluates ischemia through direct measurement of pressure beyond the coronary lesion. In contrast, the six parameters of our OPM-MCG, along with the ST-segment fluctuation scores (AUC=0.835) and Bull's eye analysis (AUC=0.914) employed by Park, offer a non-invasive alternative. According to Park JW et al, the TT segment, defined as the position from one-third of the T max amplitude (T onset) to T max (T peak), is a more effective parameter for analyzing MCG signals due to its superior signal-to-noise ratio in reflecting ventricular repolarization electrical activity ^[17]. In terms of the selected parameters, consistent with earlier literature ^[18], we focused on assessing the overall homogeneity of the repolarization process, including spatial structural similarity and smoothing of current changes. Park et al. utilized ST-segment fluctuation scores and Bull's eye analysis to evaluate the uniformity of the repolarization process in relation to current variations and spatial distribution variances for ischemia assessment. In our study, we further characterized the images by incorporating the  $\delta Ag_{sum}$ -C,  $\delta Ps_{sum}$ -PP,  $\delta Ar_{sum}$ -N and Rto $Ar_{max}$ -PN parameters of the model to analyze changes in currents, pole locations, and areas. Additionally, describing the images using the parameters of the 6 different angular points provided a comprehensive description and response to the images. In terms of practical clinical application, Park JW et al. used a 64-channel axial gradiometer system with greater channel capacity and higher sensitivity for positional discrimination, but required patients to complete two MCG tests in stress and rest states in a shielded room. Conversely, OPM-MCG does not mandate a shielded room and can effectively diagnose myocardial ischemia resulting from coronary 

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211	artery borderline lesions in the rest state, which improves the generalizability in clinical application.
212	Non-invasive methods like PET/CT, SPECT and CMR are accurate for assessing myocardial
213	ischemia, but their use is limited due to cost, long wait times and radioactive substances ^[19] . In a
214	prospective study done by Roel S. et al. [20], which included 189 patients in a head-to-head comparison,
215	it was found that using FFR as the gold standard, the sensitivity of SPECT, PET/CT, and CMR was only
216	67%, 81%, and 66%, and the specificity was only 61%, 65%, and 62%. The diagnostic accuracy of
217	PET/CT was not statistically different from that of SPECT and CMR. Recently CT-derived fractional
218	flow reserve (CT-FFR) has emerged as a noninvasive test for detecting myocardial ischemia, with a
219	sensitivity of 89% and specificity of 91% according to a multicenter study [21]. The widespread use of
220	CT-FFR has limitations including the need for good image quality and inability to assess microvascular
221	and diffuse lesions [22]. ECG is widely used in the clinic as the fastest and low-cost test. ECG uses a two-
222	dimensional linear approach to record cardiac radial currents to detect ischemia, but it can be affected
223	by body tissues or fluids and has low spatial resolution. MCG detects and measures weak magnetic
224	fields generated by the electrical activity of the heart, and the waveform of the MCG wavefrom is similar
225	to that of the ECG signal. However, MCG is less affected by changes in conductivity and does not suffer
226	from skin electrode contact problems. In addition, MCG is more sensitive to magnetic fields generated
227	by tangential currents that are more affected by myocardial ischemia, and MCG detects eddy currents
228	that are not apparent with ECG [23]. Thus, previous studies have demonstrated that MCG has a higher
229	sensitivity to early myocardial ischemia [24,25]. In most studies of MCG detection of myocardial ischemia,
230	researchers have categorized the analysis of MCG into morphological and quantitative data analyses [26].
231	Morphological analysis often focuses on amplitude, nondipole phenomena, and current or magnetic field
	11

angle. Quantitative data analysis is mostly based on changes in the magnetic field during ventricular repolarization, usually at the end of the ST segment (before the T wave) and/or during the T wave, and partially measured during the QT and QRS segment. These parameters describe the poles, the angles of the magnetic and current fields, and the waveform amplitude by extrema, dynamics, and ratios. Current studies analyzing MCG at rest for the detection of myocardial ischemia use a variety of methods, including dichotomous classification methods based on MCG parameters, quantification of abnormal MCG parameters, creation of composite indices using MCG parameters, and the application of machine-learning methods ^[27].

This is similar to our finding that a positive OPM-MCG scan was demonstrated by one or more abnormalities in the TT segment, including changes in TT segment parameters and changes in image (non-dipole phenomena and angular deflection of currents or magnetic fields). Different MCG parameters and combinations of parameters can provide more incremental information on cardiovascular disease. In addition, studies have shown that MCG is capable of accurately diagnosing myocardial ischemia resulting from epicardial coronary artery disease as well as effectively detecting myocardial ischemia caused by coronary microvascular dysfunction (CMD). The accuracy of MCG identification of CMD is 94.8%, sensitivity of 100%, and specificity of 93.3% ^[28]. In our study, we also found a small number of FFR-negative patients with positive MCG scans as described above, and considered the possibility of CMD. In the future, we will summarize the characteristic images of patients with CMD and further explore the incremental information provided by the MCGs for these patients. The difference between SQUID-based and OPM-based MCG systems depends on their sensor Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

technology. SQUID-based MCGs were developed earlier and offer high sensitivity. But their reliance

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> on liquid helium refrigeration for achieving low-temperature superconductivity, as well as the high maintenance costs associated with them, have hindered their widespread adoption and utilization. In contrast, the OPM-MCG operates at room temperature without liquid helium cooling and offers comparable sensitivity, is easier to use and less expensive to operate ^[29,30]. However, the OPM-MCG also suffers from the problem of being unsuitable for claustrophobic patients. Furthermore, the development of OPM-MCG is late, resulting in a lack of established guidelines for analyzing MCG parameters. As such, we intend to conduct further exploratory studies on OPM-MCG in various clinical settings.

> MCG has been proved to be in good concordance with FFR in the preoperative assessment of myocardial ischemia in patients with borderline coronary artery lesions, and more clinical information can be provided to patients with cardiovascular disease through more studies in the future. MCG is expected to be used for the preoperative assessment of lesion-specific ischemia in patients with borderline coronary arteries, and to reduce the number of unnecessary invasive coronary arteriography examinations. This will effectively reduce the pressure on national healthcare expenditures and reduce the burden on patients with cardiovascular diseases.

269 Limitation

The study is a single-center registry study with some limitations. We are aware that the current diagnostic model may suffer from overfitting and therefore the conclusions of this study await further validation in multicenter studies. In addition, the color coding we are currently using differs from the Rome Biomag Conference in 1981 standard, whereas there are currently multiple types of MCGs

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2		
3 4 5	274	globally, and the current methodology for analyzing myocardial ischemia has not been compared head-
6 7	275	to-head with other MCG devices.
8 9 10	276	
11 12 13	277	Conclusion
14 15	278	MCG shows excellent sensitivity, specificity, and diagnostic accuracy in identifying significant
16 17 18	279	coronary artery disease when compared to FFR. MCG can provide the evidence for a precise diagnostic
19 20 21	280	strategy for patients with borderline coronary lesions before CAG, reducing unnecessary invasive
22 23	281	examination.
24 25 26	282	
27 28 29	283	Ethics approval and consent to participate
30 31	284	This study was performed in accordance with the principles of the Declaration of Helsinki. This study
32 33 34	285	was approved by the ethics committee of Beijing Anzhen Hospital, Capital Medical University
35 36 27	286	(KS2023008). Written informed consent was required for participation in the study.
37 38 39	287	
40 41 42	288	Competing interests
43 44	289	The authors declare that they have no conflicts of interest.
45 46 47	290	
48 49 50	291	Funding
51 52	292	This study was supported by Sponsored by Beijing Nova Program (20220484222), Capital's Funds for
53 54 55	293	Health Improvement and Research (2024-2-2066), 'Deng Feng' Training Program (DFL20220603),
56 57 58 59 60	294	Beijing Hospitals Authority 'sailing' Program (YGLX202323) and Project of The Beijing Lab for 14

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29	96	
29	97	Author Contribution Statement
29	98	Xiantao Song and Chenchen Tu acted as guarantors. Xiantao Song, Chenchen Tu and Hongjia Zhang
2	99	helped to conceive the topic and revised the article. Shuwen Yang and Lanxin Feng wrote the manuscript
3	00	and finished the statistics, Mingduo Zhang, Min Zhang, Jiqiang He, Yanlong Ren, Yawei Luo and Feng
3	01	Xu contributed to the data collection. Zhao Ma, Huan Zhang, Yazhe Zhang, Linqi Liu, Shu Zhou, Xin
30	02	Zhao, and Xueyao Yang helped with data analysis. All authors read and approved the final manuscript.
30	03	
3	04	Acknowledgments
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3	06	Jinfan Tian, and Yulong Xue for their help in data collection.
3	07	
3	08	Patient and Public Involvement
30	09	Patients make more people aware of the clinical role of the MCG and how it is examined by forwarding
3	10	news stories and sharing information about clinical studies with others
3	11	
3	12	Abbreviations
3	13	AUC= area under the receiver operating characteristic curve
3	14	CCTA= coronary computed tomography angiography
3	15	CI= confidence intervals
		15

1 2		
3 4 5	316	FFR= fractional flow reserve
6 7	317	CAG= coronary angiography
8 9 10	318	NPV= negative predictive value
11 12 13	319	OPM-MCG= optical pumped magnetometer magnetocardiography
14 15	320	OR= Odds ratio
16 17 18	321	PPV= positive predictive value
19 20 21	322	ROC= receiver-operating characteristic
22 23	323	
24 25 26	324	Availability of data and materials
27 28	325	The data that support the findings of this study are available on request from the corresponding author,
29 30 31	326	Xiantao Song, upon reasonable request.
32 33 34	327	
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MCG Parameters	Definitions
	The maximum magnetic field angle at intervals of a certain time $\tau$ within TT
MAgmax-TT	
	segment
CAgmax-TT	The maximum current angle at intervals of a certain time $\tau$ within TT segment
dAgsum-C	The sum of changes in current angle at intervals of a certain time $\tau$ within TT

Table 1 The definitions of the MCG parameters

	segment
SDaarum DD	The sum of changes in the position of the positive pole point at intervals of a
oPssum-PP	certain time $\tau$ within TT segment
S A roum N	The sum of changes in negative pole area at intervals of a certain time $\tau$ within
OAISUIII-IN	TT segment
SD to Armov	The maximum value of changes in the ratio of positive to negative area at intervals
ontoAmiax	of a certain time $\tau$ within TT segment

TT= from T onset to T peak; C= current; PP= positive pole point; P= positive pole; N= negative pole;

Ag= angle; Ar= area; Rto= ratio;  $\delta$ = Change value.  $\tau$ = one tenth of the time interval between TT segment. 

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## **Figure legend**

Figure 1. Flowchart of the study design.

Figure legend: CCTA= coronary computed tomography angiography; MCG=magnetocardiography;

ICA= invasive coronary angiography; FFR=fractional flow reserve; PCI= percutaneous coronary

intervention.

Figure 2 Schematic diagram of OPM-MCG scan.

Figure legend: (A) Schematic diagram of MAg_{max}-TT and CAg_{max}-TT In magnetic field distribution maps and current density maps, the definition rule for angle values is based on the horizontal axis,

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> with counterclockwise angles being negative and clockwise angles being positive. MAgmax-TT is the maximum angle between the line connecting the maximum positive and negative magnetic poles and the horizontal axis. in the TT segment. CAg_{max}-TT is the maximum value of the angle between the current vector and the horizontal axis. in the TT segment. (B)Normal OPM-MCG scan The OPM-MCG scan showed no evidence of ischemia or obstructive coronary artery disease, as demonstrated by the lack of significant current deviations within the myocardium and absence of angle shift between the positive red pole and negative blue pole between T wave onset (T-onset) and T wave peak (Tpeak), FFR-positive and FFR-negative OPM-MCG scan and ICA Images. (C) The OPM-MCG scan of a patient in his 70s showed magnetic field angular deflection, abnormal magnetic field distribution of the positive and multipolarisation of negative poles, suggesting significant myocardial ischemia, and the ECG showed no significant abnormality. The ICA showed two lesions: 60% stenosis of the D1, 50% stenosis of the R-PDA, ... The FFRs were 0.77 for the R-PDA. (D) The OPM-MCG scan of a patient in their 60s showed no myocardial ischemia, ECG showed no significant abnormalities, echocardiography showed widening of the ascending aorta and aortic sinus. ICA showed 75% stenosis of the LAD, 60% stenosis of the RCA, FFR value of the LAD was 0.88.

MCG= magnetocardiography; FFR= fractional flow reserve ; ICA= invasive coronary angiography; D1= Diagonal branches ; R-PDA : Posterior descending artery ; LAD= Left Anterior descending artery; RCA= right coronary artery.

Figure 3. Nomogram of the diagnostic model.

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Figure legend: The nomogram graphically demonstrates the diagnostic model of OPM-MCG. Points for  $MAg_{max}$ -TT,  $CAg_{max}$ -TT,  $\delta Ag_{sum}$ -C,  $\delta Ps_{sum}$ -PP,  $\delta Ar_{sum}$ -N and  $RtoAr_{max}$ -PN can be obtained using a point caliper and then summed to obtain a total score that can be obtained using a point caliper and then summed to obtain a total score that can be measured with diagnosing myocardial ischemia in patients with borderline coronary lesions.

Figure 4 Accuracy and internal validation of the diagnostic model.

Figure legend: (A) ROC curves and 95% confidence intervals. After 500 bootstrap replications, the area under the curve and 95% confidence interval for receiver operating characteristic is 0.87 (0.809-0.932). (B) Calibration curve for the diagnostic model. Calibration curve for the borderline lesion ischemia diagnostic model was established by comparing the observed and predicted probability of a positive FFR in patients with borderline lesions of the coronary arteries. The smaller the distance of the scatter from the dashed line, the better the calibration. (C) Decision curve analysis (DCA) for diagnostic models of ischemia in borderline coronary lesions. None: net benefit when it is assumed that no patients with critical lesions of the coronary arteries would have the outcome (FFR-positive). All: net benefit when all patients with critical coronary lesions are assumed to have an outcome (FFR-positive). model: net benefit of managing critical coronary lesions with a diagnosis of myocardial ischemia based on the diagnostic model estimate. The strategy with the highest net benefit at any given threshold is the preferred strategy.

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58 59 60	23





#### Figure 2 Schematic diagram of OPM-MCG scan

Figure legend: (A) Schematic diagram of MAgmax-TT and CAgmax-TT In magnetic field distribution maps and current density maps, the definition rule for angle values is based on the horizontal axis, with counterclockwise angles being negative and clockwise angles being positive. MAgmax-TT is the maximum angle between the line connecting the maximum positive and negative magnetic poles and the horizontal axis. in the TT segment. CAgmax-TT is the maximum value of the angle between the current vector and the horizontal axis. in the TT segment. (B)Normal OPM-MCG scan The OPM-MCG scan showed no evidence of ischemia or obstructive coronary artery disease, as demonstrated by the lack of significant current deviations within the myocardium and absence of angle shift between the positive red pole and negative blue pole between T wave onset (T-onset) and T wave peak (T-peak), FFR-positive and FFR-negative OPM-MCG scan and ICA Images. (C) The OPM-MCG scan of a patient in his 70s showed magnetic field angular deflection, abnormal magnetic field distribution of the positive and multipolarisation of negative poles, suggesting significant myocardial ischemia, and the ECG showed no significant abnormality. The ICA showed two lesions: 60% stenosis of the D1, 50% stenosis of the R-PDA, . The FFRs were 0.77 for the R-PDA. (D) The OPM-MCG scan of a patient in their 60s showed no myocardial ischemia, ECG showed no significant abnormalities, echocardiography showed widening of the ascending aorta and aortic sinus. ICA showed 75% stenosis of the LAD, 60% stenosis of the RCA, FFR value of the LAD was 0.88.

1 2 3 4	MCG= magnetocardiography; FFR= fractional flow reserve ; ICA= invasive coronary angiography; D1= Diagonal branches ; R-PDA : Posterior descending artery ; LAD= Left Anterior descending artery; RCA=
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7	1074x1201mm (96 x 96 DPI)
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Points	0	10	2	0	30	40	50	60	) 7	0 8 	30	90	100
Mag _{max} _TT	-150	-10	0 -	50	0	50	1	00	150				
Cag _{max_} TT	-150	-100	-50	Ó	50	100	150	200					
$\delta Ag_{sum}$ C	ō	50	100	150	200	250	300	350	400	450			
$\delta Ps_{sum}PP$	ó	50	100 1	50 20	0 250	300	350 4	400 45	50 500				
δAr _{sum} _N	0	10	*10 ³	20*10	³ 3(	0*10 ³	40*10	D ³	50*10 ³	60*10	3		
RtoAr _{max} _PPNP	0	5*10 ³	0.05	103	25*10 ³	35*	10 ³ 0.15	45*10 ³	0.2	*10 ³	65*10 ³		0.3
Total Points	0		50	100	1	150	200		250	300	3	50	400
Diagnostic possibility			0.2	0.4 0.6	0.8	)							

Figure 3. Nomogram of the diagnostic model.

Figure legend: The nomogram graphically demonstrates the diagnostic model of OPM-MCG. Points for MAgmax-TT, CAgmax-TT, δAgsum-C, δPssum-PP, δArsum-N and RtoArmax-PN can be obtained using a point caliper and then summed to obtain a total score that can be obtained using a point caliper and then summed to obtain a total score that can be measured with diagnosing myocardial ischemia in patients with borderline coronary lesions.

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#### Figure 4 Accuracy and internal validation of the diagnostic model.

Figure legend: (A) ROC curves and 95% confidence intervals. After 500 bootstrap replications, the area under the curve and 95% confidence interval for receiver operating characteristic is 0.87 (0.809-0.932). (B) Calibration curve for the diagnostic model. Calibration curve for the borderline lesion ischemia diagnostic model was established by comparing the observed and predicted probability of a positive FFR in patients with borderline lesions of the coronary arteries. The smaller the distance of the scatter from the dashed line, the better the calibration. (C) Decision curve analysis (DCA) for diagnostic models of ischemia in borderline coronary lesions. None: net benefit when it is assumed that no patients with critical lesions of the coronary arteries would have the outcome (FFR-positive). All: net benefit when all patients with critical coronary lesions are assumed to have an outcome (FFR-positive). model: net benefit of managing critical coronary lesions with a diagnosis of myocardial ischemia based on the diagnostic model estimate. The strategy with the highest net benefit at any given threshold is the preferred strategy.

590x677mm (120 x 120 DPI)

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9 10	Assessment of myocardial ischemia in borderline coronary artery lesions based on ontical numred magnetometer	
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12	magnetocardiography	
13		
14	Shuwen Yang1#, Lanxin Feng 1#, Zhao Ma1, Huan Zhang1, Yazhe Zhang2, Linqi Liu1, Shu Zhou1, Xin Zhao1, Xingi ao Yang1, Mingduo Zhang1,	
15	Min Zhang1, Jigiang He1, Yanlong Ren1, Yawei Luo1, Feng Xu1, Xiantao Song1*, Chenchen Tu1*, Hongjia Zhang 🛱 🗟	
16	#These authors contributed equally to this work	
17	These autions contributed equally to this work.	
18	Thepartment of Cardiology, Beijing Anzhen Hospital, Capital Medical University, 100029, Beijing, China	
19	2Department of Cardiac Surgery, Beijing Anzhen Hospital, Capital Medical University, 100029, Beijing, China	
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26	The post-processing process of MCG signals is as follows. Firstly, a composite gradient magnetometer array is constructed using a separate	
27	environmental monitoring channel, and the common mode projection components of the monitoring channel are subtracted from the MCG detection	
28	array channels, effectively suppressing environmental magnetic field drift and power frequency interference. Then not not solve the 50Hz power	
29	frequency and its harmonic components of the data, and performing a 1-40Hz bandpass filter to further remove pawer frequency interference and	
30	limit the bandpass frequency to the main frequency range of the MCG. Finally, the denoised data is subjected to Repeat detection and recognition.	
32	with an average beartheat evale of 00 seconds as the length of the slice time, and the identified <b>P</b> neak point is used as the slice time alignment point to	
33	with an average nearboar cycle of 90 seconds as the length of the snee time, and the identified R-peak point is user as the time angliment point to	
34	slice the data and overlay it for average.	
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Supplementary Figure 1 Graphical Abstracts: Diagnostic Model of Myocardial Ischemia in Borderline Coronary gree Lesions Based on Optical Pumped Magnetometer Magnetocardiography

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CCTA= coronary computed tomography angiography; MCG=magnetocardiography; CAG= invasive coronary angiography; FFR=fractional flow reserve; PCI= percutaneous coronary intervention.




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ters and Definitions
of changes in magnetic field angle at intervals of a certain time $\tau$ with segment
of changes in magnetic field angle at intervals of a certain time $\tau$ with $\vec{a}$ T g segment
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a magnetic field angle at intervals of a certain time $\tau$ within TT segmers $\vec{a}$
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n of changes in magnetic pole distance at intervals of a certain time t within TT segment
n magnetic pole distance at intervals of a certain time $\tau$ within TT segment
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n of changes in current angle at intervals of a certain time $\tau$ within T $\mathbf{E}$
a current angle at intervals of a certain time $\tau$ within TT segment
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n of changes in the position of the current angle at intervals of a certain $\frac{1}{2}$ model $\tau$ within TT segment
In the position of the current angle at intervals of a certain time $\tau$ with $\vec{B}$ T segment
of changes in negative pole point area at intervals of a certain time $\tau$ with TT segment
of changes in negative pole point area at intervals of a certain time $\tau$ with TT segment
n of changes in negative pole point area at intervals of a certain time TE within TT segment
a negative pole point area at intervals of a certain time $\tau$ within TT s $\frac{1}{2}$ must be the set of the se
re pole point area between T-begin and T-peak
of the negative pole point area at intervals of a certain time $\tau$ within $\vec{E}$ s ment
of the negative pole point area at intervals of a certain time $\tau$ within $T \in \mathbb{R}$ ment
of changes in the position of the negative pole point at intervals of a certain tagene $\tau$ within TT segment
a of changes in the negative of the positive pole point at intervals of a certain the $\tau$ within TT segmen
In the position of the negative pole point at intervals of a certain time $\tau$ within TT segment
of changes in negative pole area at intervals of a certain time $\tau$ within TT $\mathbf{\underline{g}}$ egment
of changes in negative pole area at intervals of a certain time $\tau$ within TT $\overline{\mathbf{s}}$
n of changes in negative pole area at intervals of a certain time $\tau$ within $\mathbf{B}$ segment

Parameters	Definition
δ Ag _{max} -M	The maximum value of changes in magnetic field angle at intervals of a certain time $\tau$ with TA segment
δ Ar _{sum} -N	The sum of changes in negative pole area at intervals of a certain time $\tau$ within TT segments $\mathbf{S}$
δ Ar _{bp} -N	The change in nagative pole area between T-begin and T-peak
Ar _{max} -N	The maximum value of the negative pole area at intervals of a certain time $\tau$ within TT segment
Ar _{min} -N	The minimum value of the negative pole area at intervals of a certain time $\tau$ within TT segments
δ ArRto _{max} -PN	The maximum value of changes in the ratio of positive and negative pole area at intervals $\vec{a}$ ertain time $\tau$ within segment
$\delta$ ArRto _{min} -PN	The minimum value of changes in the ratio of positive and negative pole area at intervals $a = \frac{1}{2} a = \frac{1}{2}$ within segment
$\delta$ ArRto _{std} -PN	The standard deviation of changes in the ratio of positive and negative pole area at intervals $\vec{a}$
$\delta$ ArRto _{sum} -PN	The sum of changes in the ratio of positive and negative pole area at intervals of a certain time within TT segment
δ Ar _{max} -PP	The maximum value of changes in positive pole point area at intervals of a certain time $\tau$
$\delta Ar_{min}$ -PP	The minimum value of changes in positive pole point area at intervals of a certain time $\tau$ with TT segment
$\delta Ar_{std}$ -PP	The standard deviation of changes in positive pole point area at intervals of a certain time 🛛 🖬 🖞 🖞 The segment
$\delta Ar_{sum}$ -PP	The sum of changes in positive pole point area at intervals of a certain time $\tau$ within TT segment
δ Ar _{bp} -PP	The change in positive pole point area between T-begin and T-peak
Ar _{max} -PP	The maximum value of the positive pole point area at intervals of a certain time $\tau$ within Transformer segment
Ar _{min} -PP	The minimum value of the positive pole point area at intervals of a certain time $\tau$ within T $\mathbf{\overline{z}}$ segment
$\delta Ps_{max}$ -PP	The maximum value of changes in the position of the positive pole point at intervals of a certain time $\tau$ within TT seg
$\delta \mathbf{P} \mathbf{S}_{std}$ -PP	The standard deviation of changes in the position of the positive pole point at intervals of a certain $\overline{s}$ in $\overline{s}$ intervals $\tau$ within TT seg
$\delta Ps_{sum}$ -PP	The sum of changes in the position of the positive pole point at intervals of a certain time $\tau$ within TT segment
δ Ar _{max} -P	The maximum value of changes in positive pole area at intervals of a certain time $\tau$ within $f$ T gement
$\delta Ar_{min}$ -P	The minimum value of changes in positive pole area at intervals of a certain time $\tau$ within TT segment
$\delta Ar_{std}$ -P	The standard deviation of changes in positive pole area at intervals of a certain time $\tau$ within T as segment
$\delta Ar_{sum}$ -P	The sum of changes in positive pole area at intervals of a certain time $\tau$ within TT segment
δ Ar _{bp} -P	The change in positive pole area between T-begin and T-peak
Ar _{ma} x-P	The maximum value of the positive pole area at intervals of a certain time $\tau$ within TT segmen
Ar _{min} -P	The minimum value of the positive pole area at intervals of a certain time $\tau$ within TT segment

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Parameters	Definition	right, i	024-08
δ Ag _{max} -M	The maximum value of changes in magnetic field angle at intervals of a certain time $\tau$ with	<u>si</u> Sin Ti	a segment
MAg _{max} -TT	The maximum magnetic field angle at intervals of a certain time $\tau$ within TT segment	idin	
CAg _{max} -TT	The maximum current angle at intervals of a certain time $\tau$ within TT segment	iq fo	1 26
MAg _{min} -TT	The minimum magnetic field angle at intervals of a certain time $\tau$ within TT segment	т ц	O ct
CAg _{min} -TT	The minimum current angle at intervals of a certain time $\tau$ within TT segment	Ense Ses	obe
MAg-Rp	The magnetic field angle of the R-peak	eign rela	ř 20
$RtoAm-R_{p}T_{p}N$	The ratio of magnetic field amplitude at R-peak and the negative amplitude at T-peak	teme	24.
$RtoAm_R_T_P$	The ratio o magnetic field amplitude at R-neak and the positive amplitude at T-neak	tote	
Rto Am D T	The ratio of magnetic field amplitudes at <b>D</b> mask and <b>T</b> mask	int a	
$RIOAIII - R_p I_p$	The ratio of magnetic field amplitudes at R-peak and 1-peak	Ind	ade
MAg-Rp1p	The magnetic field angle between R-peak and T-peak	data	d fre
MAg-1p	The magnetic field angle of the 1-peak	n E	
CAg _{max} -Tp	The maximum current angle at T-peak	nin S	
Rto Am. Th	The ratio of positive to negative magnetic field amplitude at T-peak	<u>o</u> .	2
TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT		⋗	
$\frac{TT}{t = \text{Distance, Ps} = 1}$	The interval from the beginning of the T-wave to its peak within the cardiac cycle = Position, Ag = Angle, Am = Magnitude, Ar = Area, Rto = Ratio, P = Positive, Positive Pole = I	Al trannin	= Negative, NP = Negativ
TT TT Tt = Distance, Ps = ole, M = Magneti sgment (the positi	The interval from the beginning of the T-wave to its peak within the cardiac cycle = Position, Ag = Angle, Am = Magnitude, Ar = Area, Rto = Ratio, P = Positive, Positive Pole = I c Field, C = Current, max = Maximum, min = Minimum, sum=Sum of all, std = Standard devia on from one-third of the T max amplitude (T onset) to T max (T peak)), R _p =R peak, T _p =T peak	Al tranning, and similar technologies.	$\delta = \text{Negative, NP} = \text{Negative}$ $\delta = \text{Change value, TT} = \text{T}$

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1 2 3 4	Supplementary Table 2 Clinica	l characteristics (n = 141)		copyright, inc
		Characteristics	Total(n-141)	-ludir
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		Male n (%)	109(77.3)	or u
		$\mathbf{PMI}\left(K_{\alpha}/m^{2}\right)$	105(77.5)	ses
		Dispetes $p(0')$	$20.13\pm 3.30$	rela
		Diabetes, $\Pi(\%)$	47(33.3)	atec
		Hypercholesterolenna, II (%)	03(40.1)	ť
		Hypertension, n (%)	82(58.2)	text
		Stroke, n (%)	9(6.4)	tan
,		Smoke, n (%)	43(30.5)	d d
3		Systolic blood pressure, mmHg	128.69±15.54	ata
		Diastolic blood pressure, mmHg	75.15±10.79	min
		Heart rate	73.81±10.38	ing,
<u>)</u>		Medication, n(%)		Þ
		Aspirin	129(91.5)	trai
		Statin	137(97.2)	nin
		ACEI/ARB	45(35.6)	g, a
		SGLT2 inhibitors	22(16.7)	nd s
		Nicorandil	23(16.3)	šimi
		Admission lab results		lar t
		Low-density lipoprotein cholesterol (mmol/L)	1.82+0.69	
		hs Tnl(ng/ml)	3 5(2 5 5 8)	Inol
		Brain natriuretic pentide $(n\sigma/ml)$	29 00(14 75 48 25)	logi
↓		Blood glucose (mmol/L)	5 52(4 82 7 33)	es.
5		$Hb\Delta 1c(\%)$	6.52(7.52,7.55)	
7		ICA and FEP characteristics	0.23(3.1,1.1)	
3			50(25.5)	
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J		2-vessel disease	43(30.3)	
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2 3 4 5 6 7	3-vessel disease Number of patients with FFR≤0.8 Number of vessels with FFR Number of vessels with FFR≤0.8	48(34.0) 68(48.2) 157 74(47.1)	2024-086433 on 26 C yright, including for	
8 9 10 11 12 13	Left anterior descending artery with FFR Left circumflex artery with FFR Right coronary artery with FFR Interval between MCG and FFR	97(68.8) 25(17.7) 35(24.8) 2(1,7)	Dctober 2024. Dc Enseignement	
15         16         17         18         19         20         21         22         23         24         25         26         27         28         29         30         31         32         33         34         35         36         37         38         39         40         41         42	BMI= Body Mass Index, ACEI= angiotensin converting enzyme inhibitor, ARB = cotransporter-2 inhibitors, HbA1c= glycated hemoglobin, ICA = invasive coronary	angiotensin receptor blocker, y angiography, FFR = fraction	r, SG and data mining, Al training, and similar technologies.	
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plementary Tab	le 3 OPM-MCG parameters of	the Participant and univariab	le logistic regression model	-0864 ht, inc	
Parameters	ALL N=141	FFR-Positive N=68	FFR-Negative N=73	u ä diHagard Ratio ga bas%CD	P va
δ Ag _{max} -M	0.62 (0.44,1.19)	0.77 (0.47,5.76)	0.54 (0.43,0.72)	<b>g</b> . <b>AS</b> (1.01,1.15)	0.0
δ Ag _{min} -M	-0.34 (-0.57,-0.18)	-0.42 (-0.82,-0.28)	-0.26 (-0.42,-0.14)	<b>9</b> . <b>9</b> . <b>6</b> (0.93,1.00)	0.0
δ Ag _{std} -M	0.16 (0.11,0.68)	0.28 (0.14,2.06)	0.14 (0.10,0.20)	a.598(1.16,2.19)	<0.0
δ Ag _{sum} -M	10.6 (6.18,26.2)	20.2 (9.88,45.5)	8.28 (4.55,11.8)	<b><u><u><u></u></u></u></b> <u><u></u><u></u><u><u></u><u></u><u></u><u><u></u><u></u><u></u><u><u></u><u></u><u></u><u></u><u></u><u></u><u></u></u></u></u></u>	<0.0
δ Dt _{max} -PN	2.69 (1.97,4.12)	3.51 (2.16,12.9)	2.22 (1.89,3.16)		<0.0
$\delta Dt_{min}$ -PN	-2.20 (-3.27,-1.76)	-2.38 (-4.70,-1.91)	-2.00 (-2.80,-1.63)	0.95,1.00)	0.0
$\delta \mathbf{D} \mathbf{t}_{std}$ -PN	0.74 (0.55,1.18)	0.82 (0.63,3.45)	0.63 (0.52,0.89)	<b>1</b> . <b><u><u></u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u></b>	0.0
$\delta Dt_{sum}$ -PN	46.6 (29.1,80.7)	66.6 (42.0,110)	33.3 (25.7,48.6)	a 5 a a do 3 a do 3	<0.0
δ Ag _{max} -C	1.70 (1.21,4.83)	1.79 (1.27,9.10)	1.52 (1.16,2.98)	<b>H</b> . <b>RP</b> (1.00,1.02)	0.0
δ Ag _{min} -C	-1.24 (-3.81,0.00)	-1.70 (-8.89,-1.01)	-0.91 (-1.75,0.00)	<b>1</b> ,9 <b>8</b> (0.97,1.00)	<0.0
δ Ag _{std} -C	0.54 (0.36,1.32)	0.80 (0.37,3.16)	0.45 (0.34,0.70)	<b>▶</b> .12 (1.01,1.23)	0.0
δ Ag _{sum} -C	15.6 (9.64,38.6)	29.8 (13.5,71.6)	11.9 (7.79,17.5)	<b>a</b> .0 <b>b</b> (1.00,1.02)	<0.0
δ Ps _{max} -C	33.0 (1.00,48.8)	33.0 (1.41,125)	31.0 (1.00,34.0)	<b>1</b> .0 <b>^{<b>B</b>}</b> (1.00,1.01)	0.0
$\delta Ps_{std}$ -C	3.35 (0.24,6.16)	3.57 (0.29,11.7)	3.20 (0.24,4.86)		0.0
$\delta Ps_{sum}$ -C	39.1 (6.00,86.1)	74.4 (8.31,161)	33.4 (4.00,66.0)	<b>d</b> .0 <b>b</b> (1.00,1.01)	<0.0
δ Ar _{max} -NP	136 (74.0,220)	182 (102,314)	105 (59.0,180)	<u>.</u> .00 (1.00,1.00)	<0.0
$\delta Ar_{min}$ -NP	-84.00 (-173.00,-54.00)	-99.00 (-187.50,-62.75)	-68.00 (-148.00,-46.00)	<u>]</u> .00 <u>(</u> 1.00,1.00)	0.0
$\delta Ar_{std}$ -NP	29.6 (20.0,56.7)	31.7 (23.4,70.1)	25.7 (17.1,41.4)	<u>ප</u> .00 දී(1.00,1.01)	0.0
$\delta Ar_{sum}$ -NP	2469 (1443,4286)	3369 (2230,5728)	1672 (1277,2987)	a.00a(1.00,1.00)	<0.0
$\delta Ar_{bp}$ -NP	944 (18.0,2830)	1168 (152,3066)	626 (-46.00,2383)	<b>ğ</b> .00 <b>0</b> (1.00,1.00)	0.2
Ar _{max} -NP	3873 (3001,5765)	4269 (3260,6056)	3828 (2894,5406)	1.00 (1.00,1.00)	0.1
Ar _{min} -NP	2426 (1639,3326)	2094 (1436,3245)	2614 (2065,3360)	1.00 (1.00, 1.00)	0.0
$\delta Ps_{max}$ -NP	2.83 (2.24,4.12)	3.00 (2.24,5.28)	2.24 (2.00,3.00)	1.01 (1.00,1.01)	0.0
$\delta \mathbf{Ps}_{std}$ -NP	0.70 (0.57,1.00)	0.81 (0.65,1.20)	0.66 (0.51,0.85)	1.04 (0.98,1.11)	0.0
$\delta Ps_{sum}$ -NP	41.7 (22.2,79.9)	59.8 (39.8,104)	26.4 (20.1,51.1)	1.01,1.02)	< 0.0
$\delta \operatorname{Ar}_{\max} - N$	435 (243,750)	539 (269,990)	404 (221,526)	1.00 (1.00,1.00)	0.0

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	ALL	FFR-Positive	FFR-Negative	,∓ ∋Hangard Ratio	D 1
Parameters	N=141	N=68	N=73	ciud (25%CI)	P value
$\delta Ar_{min}-N$	-170.00 (-369.00,-25.00)	-267.00 (-565.25,-108.75)	-79.00 (-224.00,-15.00)	.00k(1.00,1.00)	< 0.00
δ Ar _{std} -N	125 (80.2,225)	160 (90.5,273)	114 (74.6,158)	<b>1</b> .00 <b>0</b> (1.00,1.01)	0.004
δ Ar _{sum} -N	12585 (7372,23204)	19058 (10208,29054)	9520 (6202,15009)	a	< 0.00
δ Ar _{bp} -N	10445 (1116,25689)	11528 (588,28595)	8107 (2900,16796)		0.840
Ar _{max} -N	53635 (43655,65410)	56546 (44597,77766)	51431 (38201,58878)	a.g0x(1.00,1.00)	0.032
Ar _{min} -N	40985 (26175,53701)	39744 (24308,59155)	40985 (29379,49923)	<b>ð.</b> <b>9</b> (1.00,1.00)	0.644
δ ArRto _{max} -PN	0.01 (0.00,0.02)	0.01 (0.00,0.03)	0.00 (0.00,0.01)	$(5.8 \times 10^{10} \text{ m})^2 = 3.426868e^{18})$	< 0.00
$\delta$ ArRto _{min} -PN	-0.02 (-0.05,-0.01)	-0.02 (-0.07,-0.01)	-0.02 (-0.040.01)	9.904(0.00.0.13)	0.134
δ ArRto _{std} -PN	0.01 (0.00,0.02)	0.01 (0.00,0.02)	0.01 (0.00,0.01)	(1.7580) $(1.7580)$ $(1.7580)$	0.114
δ ArRto _{sum} -PN	0.63 (0.32,1.72)	0.85 (0.39,2.36)	0.58 (0.29,0.88)	<b>9</b> .5 <b>4</b> (1.15,2.06)	0.014
δ Ar _{max} -PP	195 (126,404)	281 (141,704)	153 (111,286)	<b>₹</b> .0 <b>€</b> (1.00,1.00)	0.001
δ Ar _{min} -PP	-171.00 (-295.00,-106.00)	-196.00 (-563.75,-109.50)	-153.00 (-226.00,-104.00)	$\frac{1}{2}.00(1.00, 1.00)$	0.006
$\delta Ar_{std}$ -PP	54.3 (33.7,124)	77.3 (35.5,167)	43.7 (32.1,79.7)	<b>a</b> .01 <b>b</b> (1.00,1.01)	0.007
δ Ar _{sum} -PP	4689 (2685,8783)	6608 (3410,14024)	3487 (2556,5786)	<b>a</b> .00 ² (1.00,1.00)	< 0.00
δ Ar _{bp} -PP	1058 (-869.00,5166)	1360 (-872.25,5756)	737 (-869.00,4601)	<u><u><u><u></u></u>.00<u>(1.00,1.00)</u></u></u>	0.872
Ar _{max} -PP	8775 (6335,13548)	9178 (6485,14820)	8775 (6335,12776)	₹.00 <b>2</b> (1.00,1.00)	0.386
Ar _{min} -PP	5151 (2774,7571)	4626 (2618,6928)	5754 (3719,8258)	a.00 (1.00,1.00)	0.054
δ Ps _{max} -PP	3.16 (2.24,5.00)	3.61 (3.00,100)	3.00 (2.24,3.61)	<b>1</b> .01 <b>(</b> 1.00,1.02)	< 0.00
$\delta \mathbf{P} \mathbf{S}_{std}$ -PP	0.82 (0.60,1.15)	0.98 (0.66,8.50)	0.75 (0.57,0.90)	<b>g</b> .12 (1.04,1.20)	< 0.00
δ Ps _{sum} -PP	40.4 (23.1,88.6)	73.8 (29.9,195)	32.8 (21.7,54.2)	<b>3</b> .01 <b>3</b> (1.01,1.02)	< 0.00
δ Ar _{max} -P	244 (90.0,430)	312 (150,692)	172 (70.0,362)	1.00 (1.00,1.00)	0.001
δ Ar _{min} -P	-348.00 (-592.00,-203.00)	-381.00 (-812.00,-188.75)	-311.00 (-497.00,-211.00)	1.00 (1.00,1.00)	0.150
δ Ar _{std} -P	120 (80.2,203)	135 (82.3,267)	109 (75.7,159)	1.00 (1.00, 1.00)	0.105
δ Ar _{sum} -P	11899 (6525,19157)	15787 (7938,28576)	9566 (5985,15629)	1.00 (1.00, 1.00)	0.002
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	Parameters N=141		FFR-Negative N=73	n Hagard Ratio	P val
$\delta Ar_{bp}$ -P	-3600.00 (- 12686.00,2509)	-1456.00 (-14861.75,3900) -4007.00 (- 10962.00,1528) -4007.00 (- 10962.00,1528)		a.00%(1.00,1.00)	0.53
Ar _{max} -P	97097 (33699)	95392 (37311)	98685 (30122)	ka	0.56
Ar _{min} -P	89822 (63201,104875)	83948 (55748,104204)	92433 (68813,105383)	<u>a</u> <u>a</u> <u>a</u> (1.00,1.00)	0.13
MAg _{max} -TT	-62.32 (-70.64,-34.61)	-48.00 (-66.89,15.5)	-67.39 (-72.03,-53.13)	a	< 0.0
CAg _{max} -TT	45.0 (33.3,71.0)	58.2 (39.2,118)	43.1 (32.0,51.1)	<b>ð</b> . <b>927</b> (1.01,1.03)	< 0.0
MAg _{min} -TT	-70.76 (-76.85,-56.92)	-68.28 (-75.62,-41.24)	-71.98 (-77.61,-64.94)	<b>§</b> . <b>§</b> 1 <b>§</b> (1.00,1.02)	0.05
CAg _{min} -TT	32.8 (5.36,45.9)	34.7 (-10.80,63.8)	32.0 (12.3,44.0)	<b>3.90</b> (1.00,1.01)	0.47
MAg-R _p	-61.41 (-71.15,-42.88)	-53.44 (-70.66,-38.24)	-65.92 (-71.78,-50.54)	<b>d</b> . <b>9 1 1 1 1 1 1 1 1 1 1</b>	0.02
RtoAm-R _p T _p N	6.49 (4.32,9.57)	7.35 (4.92,10.4)	5.68 (3.71,8.14)	<b>a</b> .	0.02
RtoAm-R _p T _p P	7.97 (5.88,12.0)	8.66 (6.03,12.9)	7.69 (5.56,11.1)	(1.00,1.13)	0.18
RtoAm-R _p T _p	3.64 (2.38,4.70)	4.13 (3.08,5.01)	3.28 (2.36,4.50)	<b>1</b> .22 (1.04,1.43)	0.02
MAg-R _p T _p	-0.67 (-24.77,19.5)	3.61 (-25.62,33.8)	-2.72 (-22.99,13.2)	<b>a</b> .0 <b>6</b> (1.00,1.01)	0.23
MAg-T _p	-64.66 (-71.34,-45.44)	-55.82 (-70.28,-12.79)	-67.91 (-72.69,-53.13)	<b>1</b> .022(1.01,1.03)	0.00
CAg _{max} -T _p	43.1 (29.4,52.0)	45.0 (27.6,74.7)	42.2 (30.7,46.9)	.0 (1.00,1.02)	0.03
RtoAm-T _p	0.76 (0.57,1.08)	0.81 (0.52,1.22)	0.75 (0.57,0.98)	<b>4</b> .52(0.93,2.48)	0.30
RtoAm- $R_pT_pP$ RtoAm- $R_pT_pP$ MAg- $R_pT_p$ MAg- $T_p$ CAg _{max} - $T_p$ RtoAm- $T_p$ Dt = Distance, Ps = P	7.97 (5.88,12.0) $3.64 (2.38,4.70)$ $-0.67 (-24.77,19.5)$ $-64.66 (-71.34,-45.44)$ $43.1 (29.4,52.0)$ $0.76 (0.57,1.08)$ Position, Ag = Angle, Am =	8.66 (6.03,12.9) $4.13 (3.08,5.01)$ $3.61 (-25.62,33.8)$ $-55.82 (-70.28,-12.79)$ $45.0 (27.6,74.7)$ $0.81 (0.52,1.22)$ Magnitude, Ar = Area, Rto = Ra	7.69 (5.56,11.1) 3.28 (2.36,4.50) -2.72 (-22.99,13.2) -67.91 (-72.69,-53.13) 42.2 (30.7,46.9) 0.75 (0.57,0.98) atio, P = Positive, Positive Pol	$\mathbf{F}_{1.00}^{\text{min}} (1.00, 1.13)$ $\mathbf{F}_{2.2}^{\text{min}} (1.00, 1.13)$ $\mathbf{F}_{2.2}^{\text{min}} (1.00, 1.01)$ $\mathbf{F}_{2.00}^{\text{min}} (1.00, 1.02)$	<b>P</b> = ]

	D (		Diag	gnostic model	on	
	Parameters	В	OR	95%CI	15 value	
-	MAg _{max} -TT	0.011	1.011	(1.000-1.021)	₩ <u>.</u>	
	CAg _{max} -TT	0.008	1.008	(0.998-1.018)		
	$\delta Ag_{sum}$ -C	0.008	1.009	(1.000-1.019)		
	$\delta Ps_{sum}$ -PP	0.007	1.007	(1.001-1.013)		
	δAr _{sum} -N	0.001	1.001	(1.000-1.001)	<u></u>	
	RtoAr _{max} -PN	17.324	33409.498	(0.694-50738)		
l = Magnetic Field, Ag	g = Angle, max = Maxir	num, TT= T	T segment (the positi	on from one-third of the T	max angoatude (T onset	) to T n
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## Development and validation of a clinical diagnostic model for myocardial ischemia in borderline coronary lesions based on optical pumped magnetometer magnetocardiography: a prospective observational cohort study

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Development and validation of a clinical diagnostic model for myocardial ischemia in borderline coronary lesions based on optical pumped magnetometer magnetocardiography: a prospective observational cohort study Shuwen Yang1#, Lanxin Feng 1#, Mingduo Zhang1, Min Zhang1, Zhao Ma1, Huan Zhang1, Yazhe Zhang2, Linqi Liu1, Shu Zhou1, Xin Zhao1, Xueyao Yang1, Jiqiang He1, Yanlong Ren1, Yawei Luo1, Feng Xu1, Chenchen Tu1*, Xiantao Song1*, Hongjia Zhang2 #These authors contributed equally to this work. * These corresponding authors contributed equally to this work. 1Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University, 100029, Beijing, China 2Department of Cardiac Surgery, Beijing Anzhen Hospital, Capital Medical University, 100029, Beijing, China N.C. **Corresponding Author:** The first corresponding author : Dr ChenChen Tu Department of Cardiology, Anzhen Hospital, Capital Medical University, 2 Anzhen Road, Chaoyang District, 100020, Beijing, China E-mail: tcc2033@163.com Dr Xiantao Song Department of Cardiology, Anzhen Hospital, Capital Medical University, 2 Anzhen Road, Chaoyang District, 100020, Beijing, China E-mail: song0929@mail.ccmu.edu.cn Disclosures: The authors have nothing to disclose.

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#### Abstract

 **Objectives:** To develop and validate a clinical diagnostic model based on optical pumped magnetometer magnetocardiography (OPM-MCG) for the detection of myocardial ischemia in patients with borderline coronary lesions prior to invasive coronary angiography (CAG).

Design: Prospective observational cohort study.

Setting: Single center of the China National Clinical Research Center for Cardiovascular Disease (NCCMRC).

Participants: Adults with borderline coronary lesions on CAG (N=141).

Interventions: Underwent OPM-MCG before CAG and fractional flow reserve measurement.

**Results:** Five parameters were included in the final diagnostic model: MAg_{max}-TT,  $\delta Dt_{sum}$ -PN,  $\delta Ag_{sum}$ -C,  $\delta Ar_{sum}$ -N and  $\delta Ar_{min}$ -N. 1000 bootstrap replications showed that the area under the receiver operating characteristic curve (AUC) and 95% confidence interval (CI) of the diagnostic model were 0.864 (0.803-0.925), with sensitivity of 79.4%, specificity of 80.8%, positive predictive value of 79.4%, negative predictive value of 80.8%. 1000 bootstrap replications showed that the model was well-calibrated. Decision curve analysis showed a net benefit from the predictive model when the threshold probability of an ischemic patient was greater than 12%, suggesting the potential utility of the model in the real world.

**Conclusions:** A nomogram based on five OPM-MCG parameters was developed to assess myocardial ischemia in patients with borderline coronary lesions and has the potential to reduce the need for unnecessary CAG.

Trial registration number: ChiCTR2300072382.

 **Keywords:** borderline coronary lesions; optical pumped magnetometer magnetocardiography; fractional flow reserve; myocardial ischemia

## Strengths and limitations of this study

1) As a prospective observational cohort study, this study provides real-world evidence of the diagnostic performance of OPM-MCG for myocardial ischemia, enhancing the generalization of the findings.

2) The study was a single-center study, which may affect its adaptability to different settings. 3) The clinical diagnostic model did not account for myocardial ischemia due to coronary microcirculatory dysfunction and did not include evaluations performed with other MCG elle devices.

#### Introduction

Borderline coronary lesions exhibit ranging from 40% to 90% as seen in invasive coronary angiography (CAG). The FAME study ^[1] found that over 80% of lesions fell into this category, with only 35% of stenoses between 50-70% being hemodynamically significant. Predicting relevance was most accurate when estimating coronary artery diameter over 90%. Therefore, fractional flow reserve (FFR) guided intervention in patients with borderline coronary lesions (40-90% stenosis) has become a recommended treatment strategy in the 2018 ESC Interventional Guidelines ^{[2].} The 2021 ACC/AHA/SCAI Guidelines for Coronary Artery Revascularization ^[3] also provide clear recommendations for managing borderline coronary lesions: FFR and instantaneous wave-free ratio (iFR) are used to assess the need for

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percutaneous coronary intervention (PCI) in patients without evidence of ischemia but with angina and other equivalent symptoms (Class I); PCI is not recommended for stable patients with FFR >0.8 or iFR >0.89 (Class III). However, its widespread adoption in coronary catheter laboratories is hindered by its time-consuming nature, resource consumption, and potential adverse effects associated with adenosine application.

Optical pumped magnetometer magnetocardiography (OPM-MCG) measures tiny magnetic fields (10⁻¹⁵ Tesla) from the heart using atomic magnetometer technology, without radiation. It is quick, contactless, and suitable for diverse populations. Clinical studies have demonstrated that magnetocardiography (MCG) is superior to electrocardiogram (ECG) in detecting early myocardial ischemia ^[4,5,6,7] and has similar diagnostic effectiveness as SPECT for coronary artery disease (CAD) ^[8,9]. MCG was proven to be precise in diagnosing non-ST-segment elevation myocardial infarction, even in individuals who do not exhibit typical angina symptoms. ^[10,11]. However, the parameters and cut-off values of OPM-MCG that indicate myocardial ischemia in borderline coronary lesion are presently undefined.

Hence, this study aims to investigate the accuracy of OPM-MCG in diagnosing myocardial ischemia in patients with borderline coronary lesions, with invasive FFR examination serving as the reference standard.

#### Method

## **Study population**

This study was a prospective, single-center, observational, cohort study which was reviewed by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University,

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and registered with the China Clinical Trial Registry (ChiCTR2300072382). All participants signed an informed consent. The methods described in this article follow the STARD 2015 guidelines.

Participants aged 18-80 with typical angina symptoms (CCS class II or higher) or 40-90% stenosis on CCTA were scheduled for hospitalization for CAG. Exclusion criteria included: 1) Coronary artery stenosis outside of 40%-90% range on CAG; 2) Acute myocardial infarction; 3) Previous myocardial infarction; 4) Complex arrhythmias; 5) Bundle-branch block; 6) Pacemakers, metallic implants in trunk; 7) Claustrophobia.

This study was based on a prospective cohort design, the sample size of which was calculated by PASS 2021 software using the area under the receiver-operating characteristic (ROC) curve. The significance level ( $\alpha$ ) was 0.025 and the degree of certainty (1- $\beta$ ) was 0.90, combining the results of the literature review of related studies as well as the statistics of the small sample in the previous period, and calculating according to the FFR-positive (ischemic)/FFR-negative (non-ischemic) =2:3. The sample size was calculated as 138.

A total of 163 patients from June 30th to November 30th, 2023 were consecutively enrolled, and 22 patients were excluded, of which 11 patients with stenosis >90%, 7 patients underwent direct PCI without FFR testing, and 4 patients with poor quality MCG imaging, and Finally 141 patients with borderline coronary lesions underwent MCG and FFR sequentially (Figure 1). In this study, the cardiologists were not aware of the MCG results at the time of the FFR examination, and the MCG parameters were determined before the FFR examination (Supplementary Figure 1-Graphical Abstract).

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## CAG and FFR procedures

CAG and FFR measurements were performed on the vessels according to the 2021 ACC/AHA/SCAI Guidelines for Coronary Artery Revascularization and Expert consensus on the clinical pathway for FFR measurement in China. After administration of nitroglycerin, a pressure monitoring guidewire was advanced through the stenosis. Hyperemia was attained by administration of intravenous adenosine ( $140\mu g/kg/min$ ). The FFR pressure wire was positioned a minimum of 20 mm distal to the stenosis in vessel segments  $\geq 2$  mm. The presence of an FFR  $\leq 0.80$  was considered a positive indicator of functional ischemia in patients and was defined as the FFR-positive group.

## MCG imaging

The MCG recordings were conducted using a 36-channel OPM-MCG system (Miracle MCG), featuring OPM sensors sourced from Beijing X-Mag Technologies Limited's mature commercial product. The OPM sensor is based on spin-exchange relaxation free (SERF) technology, with alkali metal atoms as the core sensitive element. The OPM sensor has a sensitivity below 30 fT/Hz^{1/2}, a recording bandwidth of 1 Hz to 40 Hz, a sampling frequency of 200 Hz, and a noise baseline with not higher than 15 fT. The OPM-MCG residual magnetic field is kept below 1.5 nT, and the data acquisition mode is analog signal acquisition (Supplementary Figure 2). Each subject had a 90-second continuous recording at 36 locations ( $6 \times 6$  grid) above the chest using an arrayed sensor grid.

## MCG Signal Analysis and Statistical Analysis

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After MCG data acquisition, the software automatically post-processes the signals to generate magnetic field and current density maps and output sixty-five parameters (Supplementary Table 1). The sixty-five parameters we output characterize the stability of the current dipole in the TT segment (the position from one-third of the T max amplitude (T onset) to T max (T peak)) according to the previous studies of Park et al. and Pena et al. (see supplementary material for post-processing steps).

Statistical analysis was performed with SPSS 25.0 and R 4.3.2 (http://www.R-project.org/). Counting data were presented as numbers and percentages, while normally distributed measurement data were shown as mean  $\pm$  standard deviation. Continuous variables that were not normally distributed were presented using median and quartile values. Statistical significance was determined for all analyses with a P-value less than 0.05. Based on this cohort and the principle of at least 10 events per variable (10 EPV), we considered the rationality of the parameters included in the diagnostic model and evaluated the number of parameters. sixtyfive potential predictor variables were evaluated using univariable logistic regression, selecting those with p-values  $\leq 0.1$ . These variables were then subjected to Least Absolute Shrinkage and Selection Operator (LASSO) regression, ultimately identifying the most impactful predictors. Continuous variables representing the amount of change were transformed into ordered categorical variables based on interquartile range. Continuous variables representing absolute values were converted into dichotomous variables by grouping their upper and lower quartile values into extreme categories, while middle-range values were grouped and incorporated into the model. The final model was developed using multivariate logistic regression with a backward selection approach. The model's predictive performance was assessed using the

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enhanced bootstrap method and clinical benefit was evaluated using decision curve analysis. The MCG-FFR nomogram was used to report scores for assessing myocardial ischemia with OPM-MCG parameters.

## **Patient and Public Involvement**

Patients make more people aware of the clinical use of the OPM-MCG and how it is examined by sharing news and information about clinical studies with others.

## Result

#### **Clinical characteristics**

The study included 141 patients, mostly male (77.3%) with an average age of  $60.64 \pm 9.70$ years. After MCG scans, all patients underwent CAG and FFR examination, with 48.2% having positive FFR (FFR  $\leq 0.8$ ). A total of 157 vessels were examined, with 47.1% having FFR  $\leq 0.8$ . Interval between MCG and FFR less than 30 days, median 2 days. Most patients had FFR measurements primarily done on the LAD. See Table 1 for patient clinical characteristics.

## Selection of parameters and development of the diagnostic model

Fifty variables that were statistically significant (P < 0.1) in univariable logistic regression were included in the LASSO regression (Supplementary Table 2 and Supplementary Figure 3), and 8 variables were selected based on the reasonableness of the parameters selected to reduce the model overfitting and covariance through LASSO regression. By using the backward approach, 5 parameters were included in the final diagnostic model: MAg_{max}-TT,  $\delta Dt_{sum}$ -PN,

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 $\delta$ Ag_{sum}-C,  $\delta$ Ar_{sum}-N and  $\delta$ Ar_{min}-N (Table 2, Figure 2). The model area under the receiver operating characteristic curve (AUC) obtained from multivariate logistic regression analysis was 0.864, with sensitivity of 79.4%, specificity of 80.8%, positive predictive value of 79.4%, negative predictive value of 80.8%. The nomogram (Figure 3) provides a graphical overview of the diagnostic model using multivariate logistic regression analysis (Supplementary Table

3).

## Internal validation and net benefit of the model

The model performance for the diagnosis of myocardial ischemia in borderline coronary lesions of the OPM-MCG was evaluated by bootstrap replications. 1000 bootstrap replications showed that the model AUC and a 95% confidence interval (CI) of 0.864(0.803-0.925) (Figure 4). 1000 bootstrap replications showed that the model was well-calibrated. The mean absolute error was 0.017 (Figure 4). The decision curve analysis (DCA) for the diagnostic model showed that if the threshold probability of patients is greater than 12% (Figure 4), screening strategies based on the OPM-MCG diagnostic model resulted in superior net benefit than screen-none or screen-all strategies.

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## Discussion

CAD is presently characterized by an epicardial vascular lesion with a stenosis exceeding 50% in the CAG. Frequently, the degree of stenosis indicated by CAG is used as a reference standard for myocardial revascularization. Moreover, FFR can be used to evaluate the existence of myocardial ischemia, with a threshold of 0.8. However, as illustrated in Figure 2, the

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coronary stenosis identified in CAG may not precisely align with the FFR results. This observation is in line with the conclusions drawn in the 2019 ESC Guidelines for Chronic Coronary Syndromes ^[12,13], emphasizing that the accuracy of determining CAD solely based on angiographic stenosis was as low as 64% when compared to flow reserve fraction. The positive mismatch rate, where lesions with less than 50% stenosis may demonstrate an FFR  $\leq 0.8$ , was 19%, while the negative mismatch rate, where lesions with over 50% stenosis may result in an FFR value > 0.8, reached up to one-third. Numerous studies ^[14,15] have consistently demonstrated that FFR-guided stenting leads to superior immediate outcomes and long-term prognosis. Therefore, FFR carries a Class 1a recommendation for guiding revascularization in angiographically borderline coronary stenoses in patients with stable angina. The feasibility of diagnosing myocardial ischemia in patients with borderline coronary lesions using OPM-MCG was shown in our study, when compared to invasive FFR. The collective diagnostic potential of MCG parameters in detecting myocardial ischemia in borderline coronary lesions resulted in an AUC of 0.864 (95% CI 0.803 to 0.925). Due to factors such as time consumption, costs, patient-related discomfort, contraindications, and a lack of reimbursement, the current rate of FFR utilization in catheterization laboratories in China is less than 6% ^[3]. OPM-MCG allows ischemia assessment in patients with borderline coronary lesions prior to CAG and has a good concordance with FFR.

In comparing our MCG results with those reported by Park JW et al. ^[16], it is clear that FFR, serving as the reference standard, evaluates ischemia through direct measurement of pressure beyond the coronary lesion. In contrast, the Five parameters of our OPM-MCG, along with the ST-segment fluctuation scores (AUC=0.835) and Bull's eye analysis (AUC=0.914)

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employed by Park, offer a non-invasive alternative. According to Park JW et al, the TT segment,
defined as the interval from T onset to T peak, is a more effective parameter for analyzing MCG
signals due to its superior signal-to-noise ratio for reflecting ventricular repolarization electrical
activity ^[17] . In terms of the selected parameters, consistent with earlier literature ^[18] , we focused
on assessing the overall homogeneity of the repolarization process, including spatial structural
similarity and smoothing of current changes. Park et al. utilized ST-segment fluctuation scores
and Bull's eye analysis to evaluate the uniformity of the repolarization process in relation to
current variations and spatial distribution variances for ischemia assessment. In our study, we
further characterized the images by incorporating the $\delta Dt_{sum}$ -PN, $\delta Ag_{sum}$ -C, $\delta Ar_{sum}$ -N and $\delta$
Ar _{min} -N parameters of the model to analyze changes in currents, pole areas, and distances.
Additionally, describing the images using the parameters of the 3 different angular points
provided a comprehensive description and response to the images. In terms of image feature
discrimination, the ischemia-positive features of the OPM-MCG (pole multipolarization and
magnetic field angle deflection) initially are consistent with the FFR (Figure 2). For practical
clinical application, Park JW et al. used a 64-channel axial gradiometer system, which offers
greater channel capacity and higher sensitivity for positional discrimination. However, this
approach required patients to complete two MCG tests-one during stress and one at rest-in
a shielded room. Comparatively, OPM-MCG is equipped with a shielding barrel that can
effectively diagnose myocardial ischemia caused by borderline coronary lesions at rest, without
the need for a specially constructed shielding room. This enhances the practicality and
universality of its clinical application.

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Non-invasive methods like PET/CT, SPECT and CMR are accurate for assessing

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myocardial ischemia, but their use is limited due to cost, long wait times and radioactive substances ^[19]. In a prospective study done by Roel S. et al. ^[20], which included 189 patients in a head-to-head comparison, it was found that using FFR as the gold standard, the sensitivity of SPECT, PET/CT, and CMR was only 67%, 81%, and 66%, and the specificity was only 61%, 65%, and 62%. The diagnostic accuracy of PET/CT was not statistically different from that of SPECT and CMR. Recently, CT-derived fractional flow reserve (CT-FFR) has emerged as a noninvasive test for detecting myocardial ischemia, with a sensitivity of 89% and specificity of 91% according to a multicenter study ^[21]. The widespread use of CT-FFR has limitations including the need for good image quality and inability to assess microvascular and diffuse lesions ^[22]. ECG is widely used in the clinic as the fastest and low-cost test. ECG uses a twodimensional linear approach to record cardiac radial currents to detect ischemia, but it can be affected by body tissues or fluids and has low spatial resolution. MCG detects and measures weak magnetic fields generated by the electrical activity of the heart, and the waveform of the MCG waveform is similar to that of the ECG signal. However, MCG is less affected by changes in conductivity and does not suffer from skin electrode contact problems. In addition, MCG is more sensitive to magnetic fields generated by tangential currents that are more affected by myocardial ischemia, and MCG detects eddy currents that are not apparent with ECG^[23]. Thus, previous studies have demonstrated that MCG has a higher sensitivity to early myocardial ischemia ^[24,25]. In most studies of MCG detection of myocardial ischemia, researchers have categorized the analysis of MCG into morphological and quantitative data analyses ^[26]. Morphological analysis often focuses on amplitude, nondipole phenomena, and current or magnetic field angle. Quantitative data analysis is mostly based on changes in the magnetic

field during ventricular repolarization, usually at the end of the ST segment (before the T wave) and/or during the T wave, and partially measured during the QT and QRS segment. These parameters describe the poles, the angles of the magnetic and current fields, and the waveform amplitude by extrema, dynamics, and ratios. Current studies analyzing MCG at rest for the detection of myocardial ischemia use a variety of methods, including dichotomous classification methods based on MCG parameters, quantification of abnormal MCG parameters, creation of composite indices using MCG parameters, and the application of machine-learning methods ^[27].

This is similar to our finding that a positive OPM-MCG scan was demonstrated by one or more abnormalities in the TT segment, including changes in TT segment parameters and the changes in image (non-dipole phenomena and angular deflection of currents or magnetic fields). Different MCG parameters and their combinations can provide more incremental information on cardiovascular disease. In addition, studies have shown that MCG is capable of accurately diagnosing myocardial ischemia resulting from epicardial coronary artery disease as well as effectively detecting myocardial ischemia caused by coronary microvascular dysfunction (CMD). The accuracy of MCG identification of CMD is 94.8%, sensitivity of 100%, and specificity of 93.3% ^[28]. In our study, we also found a small number of FFR-negative patients with positive MCG scans as described above, and considered the possibility of CMD. In the future, we will summarize the characteristic images of patients with CMD and further explore the incremental information provided by the MCGs for these patients.

The difference between SQUID-based and OPM-based MCG systems lies on their sensor technology. SQUID-based MCGs were developed earlier and offer high sensitivity. But their

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reliance on liquid helium refrigeration for achieving low-temperature superconductivity, as well as the high maintenance costs associated with them, have hindered their widespread adoption and utilization. In contrast, the OPM-MCG operates at room temperature without liquid helium cooling and offers comparable sensitivity, as it is easier to use and less expensive to operate ^[29,30]. However, OPM-MCG is also unsuitable for claustrophobic patients. Furthermore, as a result of its late development, there is a lack of established guidelines for analyzing MCG parameters. As such, we intend to conduct further exploratory studies on OPM-MCG in various clinical settings.

## Limitation

The study is a single-center registry study with some limitations. We are aware that the current diagnostic model may suffer from potential overfitting and therefore the conclusions of this study require further validation in multicenter studies. In addition, the definition of positive and negative poles we currently use differs from the Rome Biomag Conference in 1981 standard, and there are currently multiple types of MCGs globally, and the current methodology for analyzing myocardial ischemia has not been compared head-to-head with other MCG devices.

## Conclusion

MCG shows excellent sensitivity, specificity, and diagnostic accuracy in identifying significant myocardial ischemia when compared to FFR. MCG can provide the evidence of a precise diagnostic strategy in patients with borderline coronary lesions before CAG, reducing

 unnecessary invasive examination.

#### Ethics approval and consent to participate

This study was performed in accordance with the principles of the Declaration of Helsinki. This study was approved by the ethics committee of Beijing Anzhen Hospital, Capital Medical University (KS2023008). Written informed consent was required for participation in the study.

## **Competing interests**

The authors declare that they have no conflicts of interest.

## **Funding statement**

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## **Author Contribution Statement**

Xiantao Song and Chenchen Tu acted as guarantors. Xiantao Song, Chenchen Tu and Hongjia Zhang helped to conceive the topic and revised the article. Shuwen Yang and Lanxin

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Feng wrote the manuscript and finished the statistics, Mingduo Zhang, Min Zhang, Jiqiang He, Yanlong Ren, Yawei Luo and Feng Xu contributed to the data collection. Zhao Ma, Huan Zhang, Yazhe Zhang, Linqi Liu, Shu Zhou, Xin Zhao, and Xueyao Yang helped with data analysis. All authors read and approved the final manuscript.

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#### Abbreviations

AUC= area under the receiver operating characteristic curve

CCTA= coronary computed tomography angiography

CI= confidence intervals

FFR= fractional flow reserve

CAG= coronary angiography

OPM-MCG= optical pumped magnetometer magnetocardiography

ROC= receiver-operating characteristic

#### Availability of data and materials

The data that support the findings of this study are available on request from the corresponding

author, Xiantao Song, upon reasonable request.

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Characteristics	Total(n=141)
Age (yrs)	60.64±9.70
Male, n (%)	109(77.3)
BMI (Kg/m2)	26.15±3.36
Diabetes, n (%)	47(33.3)
Hypercholesterolemia, n (%)	65(46.1)
Hypertension, n (%)	82(58.2)
Stroke, n (%)	9(6.4)
Smoke, n (%)	43(30.5)
Systolic blood pressure, mmHg	128.69±15.54
Diastolic blood pressure, mmHg	75.15±10.79
Heart rate	73.81±10.38
Medication, n(%)	
Aspirin	129(91.5)
Statin	137(97.2)
ACEI/ARB	45(35.6)
SGLT2 inhibitors	22(16.7)

Table 1 Clinical characteristics (n = 141)

Nicorandil	23(16.3)
Admission lab results	
Low-density lipoprotein cholesterol (mmol/L)	1.82±0.69
hs Tnl(pg/ml)	3.5(2.5,5.8)
Brain natriuretic peptide (pg/ml)	29.00(14.75,48.25
Blood glucose (mmol/L)	5.52(4.82,7.33)
HbA1c(%)	6.25(5.7,7.1)
ICA and FFR characteristics	
1-vessel disease	50(35.5)
2-vessel disease	43(30.5)
3-vessel disease	48(34.0)
Number of patients with FFR≤0.8	68(48.2)
Number of vessels with FFR	157
Number of vessels with FFR $\leq 0.8$	74(47.1)
Left anterior descending artery with FFR	97(68.8)
Left circumflex artery with FFR	25(17.7)
Right coronary artery with FFR	35(24.8)
Interval between MCG and FFR	2(1.7)

BMI= Body Mass Index, ACEI= angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker, SGLT2 inhibitors = sodium-glucose cotransporter-2 inhibitors, HbA1c=

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6	0

glycated hemoglobin, ICA = invasive coronary angiography, FFR = fractional flow reserve.

MCG Parameters	Definitions
MAg _{may} -TT	The maximum magnetic field angle at intervals of a certain time $\tau$
	within TT segment
δ Dt _{sum} -PN	The sum of changes in magnetic pole distance at intervals of a
	certain time $\tau$ within TT segment
δλα C	The sum of changes in current angle at intervals of a certain time $\boldsymbol{\tau}$
ongsum-C	within TT segment
δAr _{sum} -N	The sum of changes in negative pole area at intervals of a certain
e – sum – s	time $\tau$ within TT segment
δ <b>Δ</b> r · -N	The minimum value of changes in negative pole area at intervals of
Of Himin TV	a certain time $\tau$ within TT segment
M= Magnetic Field; Ag=	= Angle; TT= from T onset to T peak; $\delta$ = Change value; DT= Distance;

Table 2 The definitions of the MCG parameters

M= Magnetic Field; Ag= Angle; TT= from T onset to T peak;  $\delta$ = Change value; DT= Distance; PN= Positive Pole to Negative Pole; C=Current; Ar= Area; N= Negative Pole; ;  $\tau$ = one tenth of the time interval between TT segment.

## **Figure legend**

Figure 1. Flowchart of the study design.

Figure legend: CCTA= coronary computed tomography angiography;

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MCG=magnetocardiography; ICA= invasive coronary angiography; FFR=fractional flow reserve; PCI= percutaneous coronary intervention.

Figure 2 Schematic diagram of OPM-MCG scan.

Figure legend: (A) Schematic diagram of MAg_{max}-TT and current angle. In magnetic field distribution maps and current density maps, the definition rule for angle values is based on the horizontal axis, with counterclockwise angles being negative and clockwise angles being positive.  $MAg_{max}$ -TT is the maximum angle between the line connecting the maximum positive and negative magnetic poles and the horizontal axis. in the TT segment.  $\delta Ag_{sum}$ -C is the sum of changes in current angle at intervals of a certain time  $\tau$  within TT segment (B)Normal OPM-MCG scan. The OPM-MCG scan showed no evidence of ischemia or obstructive coronary artery disease, as demonstrated by the lack of significant current deviations within the myocardium and absence of angle shift between the positive red pole and negative blue pole between T-onset and T-peak. (C) The OPM-MCG scan of a patient in his 70s showed magnetic field angular deflection, abnormal magnetic field distribution of the positive and multipolarisation of negative poles, suggesting significant myocardial ischemia, and the ECG showed no significant abnormality. The CAG showed two lesions: 60% stenosis of the D1, 50% stenosis of the R-PDA. The FFRs were 0.77 for the R-PDA. (D) The OPM-MCG scan of a patient in his 60s showed no myocardial ischemia, ECG showed no significant abnormalities, echocardiography showed widening of the ascending aorta and aortic sinus. CAG showed 75% stenosis of the LAD, 60% stenosis of the RCA, FFR value of the LAD was 0.88.
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MCG= magnetocardiography; FFR= fractional flow reserve; ICA= invasive coronary angiography; D1= Diagonal branches; R-PDA= Posterior descending artery; LAD= Left Anterior descending artery; RCA= right coronary artery.

Figure 3. Nomogram of the diagnostic model.

 Figure legend: The nomogram graphically demonstrates the diagnostic model of OPM-MCG. Points for MAg_{max}-TT,  $\delta Dt_{sum}$ -PN,  $\delta Ag_{sum}$ -C,  $\delta Ar_{sum}$ -N and  $\delta Ar_{min}$ -N can be obtained using a point caliper and then summed to obtain a total score that can be measured with diagnosing myocardial ischemia in patients with borderline coronary lesions.

Figure 4 Accuracy and internal validation of the diagnostic model.

Figure legend: (A) ROC curves for the diagnostic model. After 1000 bootstrap replications, the area under the curve and 95% confidence interval for receiver operating characteristic is 0.864 (0.803-0.925). (B) Calibration curve for the diagnostic model. Calibration curve for the borderline lesion ischemia diagnostic model was established by comparing the actual and predicted probability of a positive FFR in patients with borderline lesions of the coronary arteries. The smaller the distance of the scatter from the dashed line, the better the calibration. (C) Decision curve analysis (DCA) for diagnostic models of ischemia in borderline lesions of the coronary lesions. Treat none: net benefit when it is assumed that no patients with borderline lesions of the coronary arteries would have the outcome (FFR-positive). Treat all: net benefit when all patients with borderline coronary lesions are assumed to have an outcome (FFR-positive). Diagnostic model: net benefit of managing borderline coronary lesions with a diagnosis of

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Figure legend: CCTA= coronary computed tomography angiography; MCG=magnetocardiography; ICA= invasive coronary angiography; FFR=fractional flow reserve; PCI= percutaneous coronary intervention.

510x441mm (96 x 96 DPI)



#### Figure 2 Schematic diagram of OPM-MCG scan.

Figure legend: (A) Schematic diagram of MAgmax-TT and current angle. In magnetic field distribution maps and current density maps, the definition rule for angle values is based on the horizontal axis, with counterclockwise angles being negative and clockwise angles being positive. MAgmax-TT is the maximum angle between the line connecting the maximum positive and negative magnetic poles and the horizontal axis. in the TT segment. δAgsum-C is the sum of changes in current angle at intervals of a certain time τ within TT segment (B)Normal OPM-MCG scan. The OPM-MCG scan showed no evidence of ischemia or obstructive coronary artery disease, as demonstrated by the lack of significant current deviations within the myocardium and absence of angle shift between the positive red pole and negative blue pole between T-onset and T-peak. (C) The OPM-MCG scan of a patient in his 70s showed magnetic field angular deflection, abnormal magnetic field distribution of the positive and multipolarisation of negative poles, suggesting significant myocardial ischemia, and the ECG showed no significant abnormality. The CAG showed two lesions: 60% stenosis of the D1, 50% stenosis of the R-PDA. The FFRs were 0.77 for the R-PDA. (D) The OPM-MCG scan of a patient in his 60s showed no myocardial ischemia, ECG showed no significant abnormalities, echocardiography showed widening of the ascending aorta and aortic sinus. CAG showed 75% stenosis of the LAD, 60% stenosis of the RCA, FFR value of the LAD was 0.88.

MCG= magnetocardiography; FFR= fractional flow reserve; ICA= invasive coronary angiography; D1=

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Diagonal branches; R-PDA= Posterior descending artery; LAD= Left Anterior descending artery; RCA= right coronary artery.

1090x1206mm (96 x 96 DPI)

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#### Figure 4 Accuracy and internal validation of the diagnostic model.

Figure legend: (A) ROC curves for the diagnostic model. After 1000 bootstrap replications, the area under the curve and 95% confidence interval for receiver operating characteristic is 0.864 (0.803-0.925). (B) Calibration curve for the diagnostic model. Calibration curve for the borderline lesion ischemia diagnostic model was established by comparing the actual and predicted probability of a positive FFR in patients with borderline lesions of the coronary arteries. The smaller the distance of the scatter from the dashed line, the better the calibration. (C) Decision curve analysis (DCA) for diagnostic models of ischemia in borderline coronary lesions. Treat none: net benefit when it is assumed that no patients with borderline lesions of the coronary arteries would have the outcome (FFR-positive). Treat all: net benefit when all patients with borderline coronary lesions are assumed to have an outcome (FFR-positive). Diagnostic model: net benefit of managing borderline coronary lesions with a diagnosis of myocardial ischemia based on the diagnostic model estimate. The strategy with the highest net benefit at any given threshold is the preferred strategy.

239x257mm (300 x 300 DPI)

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# **Supplementary Material**

Development and validation of a clinical diagnostic model for myocardial ischemia in borderline coronary lesions based on optical pumped magnetometer magnetocardiography: a prospective observational cohort study

# Contents

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# **OPM-MCG** post-processing steps

BMJ Open **M-MCG post-processing steps** The post-processing process of MCG signals is as follows. Firstly, a composite gradient magnetometer arranges **g**onstructed using a separate environmental monitoring channel, and the common mode projection components of the monitoring channel subtracted from the MCG detection array channels, effectively suppressing environmental magnetic field drift and power frequency interference. Then, notching the 50Hz power frequency and its harmonic components of the data, and performing a 1-40Hz bandpass filter to further remove power frequency prover frequency and its harmonic components of the data, and performing a 1-40Hz bandpass filter to frequency interference and limit the bandpass frequency to the main frequency range of the MCG. Finally, the denoised data and be everage between the length of the slice time, and the identified alignment point to slice the data and overlay it for average. interference and limit the bandpass frequency to the main frequency range of the MCG. Finally, the denoised data because to R-peak detection







CCTA= coronary computed tomography angiography; MCG=magnetocardiography; CAG= invasive coronary angiography; FFR=fractional flow reserve; PCI= percutaneous coronary intervention. iographique de l





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Parameters	Definition
δ Ag _{max} -M	The maximum value of changes in magnetic field angle at intervals of a certain time $\tau$ within Tesegment
δ Ag _{min} -M	The minimum value of changes in magnetic field angle at intervals of a certain time $\tau$ within TTP segment
δ Ag _{std} -M	The standard deviation of changes in magnetic field angle at intervals of a certain time $\tau$ within <b>F</b> T segment
δ Ag _{sum} -M	The sum of changes in magnetic field angle at intervals of a certain time $\tau$ within TT segment $\vec{x}$
δ Dt _{max} -PN	The maximum value of changes in magnetic pole distance at intervals of a certain time $\tau$ with $\vec{B}$ T segment
δ Dt _{min} -PN	The minimum value of changes in magnetic pole distance at intervals of a certain time $\tau$ with $\vec{a}$ T segment
δ Dt _{std} -PN	The standard deviation of changes in magnetic pole distance at intervals of a certain time twitting TT segment
δ Dt _{sum} -PN	The sum of changes in magnetic pole distance at intervals of a certain time $\tau$ within TT segments
δ Ag _{max} -C	The maximum value of changes in current angle at intervals of a certain time $\tau$ within TT second
δ Ag _{min} -C	The minimum value of changes in current angle at intervals of a certain time $\tau$ within TT segment
δ Ag _{std} -C	The standard deviation of changes in current angle at intervals of a certain time $\tau$ within TTZ ment
δ Ag _{sum} -C	The sum of changes in current angle at intervals of a certain time $\tau$ within TT segment
δ Ps _{max} -C	The maximum value of changes in the position of the current angle at intervals of a certain time within TT segment
δ Ps _{std} -C	The standard deviation of changes in the position of the current angle at intervals of a certain time or within TT segment
δ Ps _{sum} -C	The sum of changes in the position of the current angle at intervals of a certain time $\tau$ within TE segment
δ Ar _{max} -NP	The maximum value of changes in negative pole point area at intervals of a certain time $\tau$ within TT segment
δ Ar _{min} -NP	The minimum value of changes in negative pole point area at intervals of a certain time <b>v</b> within TT segment
$\delta Ar_{std}$ -NP	The standard deviation of changes in negative pole point area at intervals of a certain time $\tau$ situation TT segment
δ Ar _{sum} -NP	The sum of changes in negative pole point area at intervals of a certain time vithin TT segment
δ Ar _{bp} -NP	The change in negative pole point area between T-begin and T-peak
Ar _{max} -NP	The maximum value of the negative pole point area at intervals of a certain time $\tau$ within T $\vec{\mathbf{E}}$ segment
Ar _{min} -NP	The minimum value of the negative pole point area at intervals of a certain time $\tau$ within T esegenent
$\delta Ps_{max}$ -NP	The maximum value of changes in the position of the negative pole point at intervals of $\tilde{a}$ contains $\tau$ within segment
$\delta Ps_{std}$ -NP	The standard deviation of changes in the negative of the positive pole point at intervals of a cest tain time $\tau$ within segment
$\delta Ps_{sum}$ -NP	The sum of changes in the position of the negative pole point at intervals of a certain time $\tau$ with TT segment
δ Ar _{max} -N	The maximum value of changes in negative pole area at intervals of a certain time $\tau$ within TT s generation $\tau$

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Parameters	Definition
δ Ag _{max} -M	The maximum value of changes in magnetic field angle at intervals of a certain time $\tau$ within TEsegment
$\delta Ar_{min}$ -N	The minimum value of changes in negative pole area at intervals of a certain time $\tau$ within $\mathbf{\tilde{E}}$ summer summer summer summer $\tau$ within $\mathbf{\tilde{E}}$ summer sum
$\delta Ar_{std}$ -N	The standard deviation of changes in negative pole area at intervals of a certain time <b>t</b> within T Segment
δ Ar _{sum} -N	The sum of changes in negative pole area at intervals of a certain time $\tau$ within TT segment $\overline{a}_{m}$
δ Ar _{bp} -N	The change in nagative pole area between T-begin and T-peak
Ar _{max} -N	The maximum value of the negative pole area at intervals of a certain time $\tau$ within TT segneration
Ar _{min} -N	The minimum value of the negative pole area at intervals of a certain time $\tau$ within TT segn
$\delta$ ArRto _{max} -PN	The maximum value of changes in the ratio of positive and negative pole area at intervals of $\frac{1}{2}$ tain time $\tau$ within segment
$\delta$ ArRto _{min} -PN	The minimum value of changes in the ratio of positive and negative pole area at intervals of tain time $\tau$ within segment
δ ArRto _{std} -PN	The standard deviation of changes in the ratio of positive and negative pole area at intervals of $\vec{p}$ reaction time $\tau$ within segment
δ ArRto _{sum} -PN	The sum of changes in the ratio of positive and negative pole area at intervals of a certain time by within TT segment
δ Ar _{max} -PP	The maximum value of changes in positive pole point area at intervals of a certain time <b>v</b> within T segment
δ Ar _{min} -PP	The minimum value of changes in positive pole point area at intervals of a certain time <b>v</b> within <b>T</b> segment
δ Ar _{std} -PP	The standard deviation of changes in positive pole point area at intervals of a certain time 🛛 🖞 itlan TT segment
δ Ar _{sum} -PP	The sum of changes in positive pole point area at intervals of a certain time $\tau$ within TT segments
δ Ar _{bp} -PP	The change in positive pole point area between T-begin and T-peak
Ar _{max} -PP	The maximum value of the positive pole point area at intervals of a certain time $\tau$ within TT segment
Ar _{min} -PP	The minimum value of the positive pole point area at intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ within TT $\frac{3}{2}$ egreen intervals of a certain time $\tau$ with the transformation time $\tau$ and $\tau$ with the transformation time $\tau$ with the transformation time $\tau$ and $\tau$ with the transformation time $\tau$ with the transformation time $\tau$ and $\tau$ with the transformation time $\tau$ and $\tau$ with the transformation time $\tau$ and $\tau$
δ Ps _{max} -PP	The maximum value of changes in the position of the positive pole point at intervals of $abcertain time \tau$ within segment
$\delta \mathbf{Ps_{std}}\text{-}\mathbf{PP}$	The standard deviation of changes in the position of the positive pole point at intervals of a $rac{s}{r}$ tain time $\tau$ within segment
δ Ps _{sum} -PP	The sum of changes in the position of the positive pole point at intervals of a certain time $\tau$ with $\vec{k}$ TT segment
δ Ar _{max} -P	The maximum value of changes in positive pole area at intervals of a certain time $\tau$ within TT suggement
δ Ar _{min} -P	The minimum value of changes in positive pole area at intervals of a certain time $\tau$ within TT segment
	The standard deviation of changes in positive note area at intervals of a certain time. I within TT regement

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Parameters	Definition	. <del>.</del> 3	086
δ Ag _{max} -M	The maximum value of changes in magnetic field angle at intervals of a certain time $\tau$ within	₽T	Esegment
δ Ar _{sum} -P	The sum of changes in positive pole area at intervals of a certain time $\tau$ within TT segment	ding	on
δ Ar _{bp} -P	The change in positive pole area between T-begin and T-peak	for	26 C
Ar _{ma} x-P	The maximum value of the positive pole area at intervals of a certain time $\tau$ within TT segments of the term of the positive pole area at intervals of a certain time $\tau$ within TT segments of the term of the term of the term of the term of term of terms of the term of term of terms of ter	<u>ل</u> بر الر	octo
Ar _{min} -P	The minimum value of the positive pole area at intervals of a certain time $\tau$ within TT segments of the positive pole area at intervals of a certain time $\tau$ within TT segments of the positive pole area at intervals of the positive pole at the	Ĕu	ber
MAg _{max} -TT	The maximum magnetic field angle at intervals of a certain time $\tau$ within TT segment	elate	202
CAg _{max} -TT	The maximum current angle at intervals of a certain time $\tau$ within TT segment	a ne	Έ
MAg _{min} -TT	The minimum magnetic field angle at intervals of a certain time $\tau$ within TT segment	ote	Dow
CAg _{min} -TT	The minimum current angle at intervals of a certain time $\tau$ within TT segment	upe Xta	nloa
MAg-Rp	The magnetic field angle of the R-peak	nd c	idec
$RtoAm-R_pT_pN$	The ratio of magnetic field amplitude at R-peak and the negative amplitude at T-peak	r (A	1 fro
RtoAm-R _p T _p P	The ratio o magnetic field amplitude at R-peak and the positive amplitude at T-peak	BES) mini	B E
RtoAm-R _p T _p	The ratio of magnetic field amplitudes at R-peak and T-peak	ng.	tp://
MAg-RpTp	The magnetic field angle between R-peak and T-peak	₽ ŧ	
MAg-Tp	The magnetic field angle of the T-peak	rain	
CAg _{max} -Tp	The maximum current angle at T-peak	ing,	Ď.
RtoAm-Tp	The ratio of positive to negative magnetic field amplitude at T-peak	ano	<u>,</u>
TT	The interval from the beginning of the T-wave to its peak within the cardiac cycle	sin	
Dt = Distance, Ps =	= Position, Ag = Angle, Am = Magnitude, Ar = Area, Rto = Ratio, P = Positive, Positive Pole = I	n Har	<b>g</b> = Negative, NP = Negative
Pole, M = Magnet	ic Field, C = Current, max = Maximum, min = Minimum, sum=Sum of all, std = Standard devia		$\mathbf{F} \delta = \text{Change value, TT} = \text{TT}$
segment (the posit	ion from one-third of the T max amplitude (T onset) to T max (T peak)), $R_p=R$ peak, $T_p=T$ peak	ihnc	e 10
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upplementary Ta	able 2 OPM-MCG paramete	ers of univariable logistic reg	ression model P < 0.1	4-086 ght, ir	
Darameters	ALL	FFR-Positive	FFR-Negative	Gu dodds Ratio	D va
1 arameters	N=141	N=68	N=73	ing (95%CI)	1 va
δ Ag _{max} -M	0.62 (0.44,1.19)	0.77 (0.47,5.76)	0.54 (0.43,0.72)	<b>2</b> 1.0 <b>0</b> 7(1.023-1.163)	0.0
δ Ag _{min} -M	-0.34 (-0.57,-0.18)	-0.42 (-0.82,-0.28)	-0.26 (-0.42,-0.14)	kom ka	0.0
δ Ag _{std} -M	0.16 (0.11,0.68)	0.28 (0.14,2.06)	0.14 (0.10,0.20)	<u>ā</u> 24(1.213-2.313)	0.0
δ Ag _{sum} -M	10.6 (6.18,26.2)	20.2 (9.88,45.5)	8.28 (4.55,11.8)	at a 2664(1.037-1.1)	<0.0
δ Dt _{max} -PN	2.69 (1.97,4.12)	3.51 (2.16,12.9)	2.22 (1.89,3.16)	ອາສາອງຊຸ4(1.001-1.032)	0.0
$\delta Dt_{min}$ -PN	-2.20 (-3.27,-1.76)	-2.38 (-4.70,-1.91)	-2.00 (-2.80,-1.63)	<b>É É É 1</b> (0.94-0.991)	0.0
$\delta Dt_{std}$ -PN	0.74 (0.55,1.18)	0.82 (0.63,3.45)	0.63 (0.52,0.89)	BIB 88(1.031-1.332)	0.0
$\delta Dt_{sum}$ -PN	46.6 (29.1,80.7)	66.6 (42.0,110)	33.3 (25.7,48.6)	କ୍ଷ୍ମ କ୍ଷ	<0.
δ Ag _{max} -C	1.70 (1.21,4.83)	1.79 (1.27,9.10)	1.52 (1.16,2.98)		0.0
δ Ag _{min} -C	-1.24 (-3.81,0.00)	-1.70 (-8.89,-1.01)	-0.91 (-1.75,0.00)	3(0.962-0.997)	0.0
δ Ag _{std} -C	0.54 (0.36,1.32)	0.80 (0.37,3.16)	0.45 (0.34,0.70)	<b>9</b> 1:1 <b>2</b> 7(1.026-1.252)	0.0
δ Ag _{sum} -C	15.6 (9.64,38.6)	29.8 (13.5,71.6)	<b>11.9</b> (7.79,17.5)	<b>4</b> (1.006-1.025)	0.0
δ Ps _{max} -C	33.0 (1.00,48.8)	33.0 (1.41,125)	31.0 (1.00,34.0)	≝1.088(1.003-1.015)	0.0
$\delta Ps_{std}$ -C	3.35 (0.24,6.16)	3.57 (0.29,11.7)	3.20 (0.24,4.86)	ធ្វី 1.073(1.019-1.14)	0.0
$\delta Ps_{sum}$ -C	39.1 (6.00,86.1)	74.4 (8.31,161)	33.4 (4.00,66.0)	a 1. (1.005-1.015)	<0.0
$\delta Ar_{max}$ -NP	136 (74.0,220)	182 (102,314)	105 (59.0,180)	<b>ब्र</b> .00 (1.0002,1.003)	0.0
$\delta Ar_{std}$ -NP	29.6 (20.0,56.7)	31.7 (23.4,70.1)	25.7 (17.1,41.4)	jal.0 <b>8</b> 4 (1.000,1.010)	0.0
$\delta Ar_{sum}$ -NP	2469 (1443,4286)	3369 (2230,5728)	1672 (1277,2987)	1.0 <b>g</b> 02 <b>€</b> (1.00006, 1.00034)	0.0
Ar _{max} -NP	3873 (3001,5765)	4269 (3260,6056)	3828 (2894,5406)	1.00( <b>¹</b> )0.999989, 1.000213)	0.0
$\delta Ps_{sum}$ -NP	41.7 (22.2,79.9)	59.8 (39.8,104)	26.4 (20.1,51.1)	គ្នា.0រដ្ឋ3(1.006-1.021)	0.0
δ Ar _{max} -N	435 (243,750)	539 (269,990)	404 (221,526)	<b>B</b> 18001(1-1.002)	0.0
$\delta Ar_{min}$ -N	-170.00 (-369.00,-25.00)	-267.00 (-565.25,-108.75)	-79.00 (-224.00,-15.00)	0.9 <b>5</b> 8(0.996-0.999)	0.0
$\delta$ Ar _{std} -N	125 (80.2,225)	160 (90.5,273)	114 (74.6,158)	1.095(1.002-1.008)	0.0
$\delta Ar_{sum}-N$	12585 (7372,23204)	19058 (10208,29054)	9520 (6202,15009)	1.000084 (1.000046, 1.000122)	<0.0
Ar _{max} -N	53635 (43655,65410)	56546 (44597,77766)	51431 (38201,58878)	1.000014 <u>ğ</u> 1.000002, 1.000026)	0.0
δ ArRto _{max} -PN	0.01 (0.00,0.02)	0.01 (0.00,0.03)	0.00 (0.00,0.01)	4.494e+14 (5.890e+2,3.427+29)	0.0

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Parameters	ALL	FFR-Positive	FFR-Negative	in SOdds Ratio	P value
	IN-141	IN-08	IN-75		
δ ArRto _{min} -PN	-0.02 (-0.05,-0.01)	-0.02 (-0.07,-0.01)	-0.02 (-0.04,-0.01)		0.014
$\delta$ ArRto _{std} -PN	0.01 (0.00,0.02)	0.01 (0.00,0.02)	0.01 (0.00,0.01)	$3.177 \bullet +1601.758 \bullet +3,5.740 \bullet +29)$	0.015
δ ArRto _{sum} -PN	0.63 (0.32,1.72)	0.85 (0.39,2.36)	0.58 (0.29,0.88)	<b>6 6 6 6 6 6 6 6 7 7 7 7 7 7 7 7 7 7</b>	0.004
δ Ar _{max} -PP	195 (126,404)	281 (141,704)	153 (111,286)	<u>a</u> <u>a</u> <u>b</u> (1.001,1.003)	0.001
δ Ar _{min} -PP	-171.00 (-295.00,-106.00)	-196.00 (-563.75,-109.50)	-153.00 (-226.00,-104.00)	n n n n n n n n n n n n n n n n n n n	0.003
$\delta$ Ar _{std} -PP	54.3 (33.7,124)	77.3 (35.5,167)	43.7 (32.1,79.7)		0.004
δ Ar _{sum} -PP	4689 (2685,8783)	6608 (3410,14024)	3487 (2556,5786)	1.00월월 2000053, 1.000187)	< 0.001
Ar _{min} -PP	5151 (2774,7571)	4626 (2618,6928)	5754 (3719,8258)	0.999 3 4 0.999933, 1.000003)	0.06
δ Ps _{max} -PP	3.16 (2.24,5.00)	3.61 (3.00,100)	3.00 (2.24,3.61)	ລູເສັ້ນ¥ໍ1(1.005-1.019)	0.002
$\delta \mathbf{Ps}_{std}$ -PP	0.82 (0.60,1.15)	0.98 (0.66,8.50)	0.75 (0.57,0.90)		0.003
δ Ps _{sum} -PP	40.4 (23.1,88.6)	73.8 (29.9,195)	32.8 (21.7,54.2)	<b>عِنْكَةِ 2</b> (1.006-1.019)	< 0.001
δ Ar _{max} -P	244 (90.0,430)	312 (150,692)	172 (70.0,362)	ية · 1001(1-1.002)	0.007
δ Ar _{std} -P	120 (80.2,203)	135 (82.3,267)	109 (75.7,159)	<b>1</b> <u>1</u> <u></u>	0.07
δ Ar _{sum} -P	11899 (6525,19157)	15787 (7938,28576)	9566 (5985,15629)	1.000	0.001
MAg _{max} -TT	-62.32 (-70.64,-34.61)	-48.00 (-66.89,15.5)	-67.39 (-72.03,-53.13)	<b>بق</b> 1.0 <b>ي</b> 9(1.009-1.029)	< 0.001
CAg _{max} -TT	45.0 (33.3,71.0)	58.2 (39.2,118)	43.1 (32.0,51.1)	al.078(1.009-1.028)	< 0.001
MAg _{min} -TT	-70.76 (-76.85,-56.92)	-68.28 (-75.62,-41.24)	-71.98 (-77.61,-64.94)	ଞ୍ <u></u> ର୍ସ.0 <mark>ई</mark> 9(1.000-1.018)	0.052
MAg-R _p	-61.41 (-71.15,-42.88)	-53.44 (-70.66,-38.24)	-65.92 (-71.78,-50.54)	jai.0\$5(1.003-1.028)	0.017
$RtoAm-R_pT_pN$	6.49 (4.32,9.57)	7.35 (4.92,10.4)	5.68 (3.71,8.14)	g1.055(1.005-1.126)	0.064
RtoAm-R _p T _p P	7.97 (5.88,12.0)	8.66 (6.03,12.9)	7.69 (5.56,11.1)	<b>b</b> 1.( <b>b</b> )(1.004-1.133)	0.061
RtoAm-R _p T _p	3.64 (2.38,4.70)	4.13 (3.08,5.01)	3.28 (2.36,4.50)	<b>8</b> .2 <b>8</b> 7(1.047-1.445)	0.016
MAg-T _p	-64.66 (-71.34,-45.44)	-55.82 (-70.28,-12.79)	-67.91 (-72.69,-53.13)	^o 1.0 ^d <u>4</u> 5(1.006-1.026)	0.002
CAg _{max} -T _p	43.1 (29.4,52.0)	45.0 (27.6,74.7)	42.2 (30.7,46.9)	1.029(1.001-1.017)	0.037
RtoAm-T _p	0.76 (0.57,1.08)	0.81 (0.52,1.22)	0.75 (0.57,0.98)	1.559(0.978-2.618)	0.095
Dt = Distance, Ps	= Position, Ag = Angle, Am =	Magnitude, Ar = Area, Rto =	Ratio, $P = Positive$ , Positive	Pole = PP, Not Negative, NP = Nega	tive

Dt = Distance, Ps = Position, Ag = Angle, Am = Magnitude, Ar = Area, Rto = Ratio, P = Positive, Positive Pole = PP, Imperiative, NP = NegativePole, M = Magnetic Field, C = Current, max = Maximum, min = Minimum, sum=Sum of all, std = Standard deviationsegment (the position from one-third of the T max amplitude (T onset) to T max (T peak)), R_p=R peak, T_p=T peakFor peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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2 3	Supplementary Table 3 Diagnostic model for	or assessment o	f myocardial isch	emia in borderline coronary	artery legions	
4 5			Di	agnostic model	6433 ħclu	
6	Parameters	В	OR	95%CI	15 value	
7	MAg _{max} -TT	1.385	3.995	(1.592-10.023)	<b>B</b> .003	
8 9	δDt _{sum} -PN	0.671	1.956	(1.270-3.012)	\$.A0	
10	$\delta Ag_{sum}$ -C	0.411	1.508	(0.989-2.298)	80.80 180.56	
11	δAr _{sum} -N	0.641	1.899	(1.251-2.883)		
12	δAr _{min} -N	0.515	1.674	(1.121-2.500)		
14	M= Magnetic Field; Ag= Angle; TT= from T	onset to T peal	k; δ= Change valu	e; DT= Distance; PN= Positiv	ve Pore te Nega	tive Pole; C=Current;
15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33	Ar= Area; N= Negative Pole; ; τ= one tenth o	f the time interv	al between TT seg	nent.	nloaded from http://bmjopen.bmj.com/ on June 10, 202 uperieur (ABES) . xt and data mining, Al training, and similar technologie	
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# **BMJ Open**

# Development and validation of a clinical diagnostic model for myocardial ischemia in borderline coronary lesions based on optical pumped magnetometer magnetocardiography: a prospective observational cohort study

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Development and validation of a clinical diagnostic model for myocardial ischemia in borderline coronary lesions based on optical pumped magnetometer magnetocardiography: a prospective observational cohort study Shuwen Yang1#, Lanxin Feng 1#, Mingduo Zhang1, Min Zhang1, Zhao Ma1, Huan Zhang1, Yazhe Zhang2, Linqi Liu1, Shu Zhou1, Xin Zhao1, Xueyao Yang1, Jiqiang He1, Yanlong Ren1, Yawei Luo1, Feng Xu1, Chenchen Tu1*, Xiantao Song1*, Hongjia Zhang2 #These authors contributed equally to this work. * These corresponding authors contributed equally to this work. 1Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University, 100029, Beijing, China 2Department of Cardiac Surgery, Beijing Anzhen Hospital, Capital Medical University, 100029, Beijing, China N.C. **Corresponding Author:** The first corresponding author : Dr ChenChen Tu Department of Cardiology, Anzhen Hospital, Capital Medical University, 2 Anzhen Road, Chaoyang District, 100020, Beijing, China E-mail: tcc2033@163.com Dr Xiantao Song Department of Cardiology, Anzhen Hospital, Capital Medical University, 2 Anzhen Road, Chaoyang District, 100020, Beijing, China E-mail: song0929@mail.ccmu.edu.cn Disclosures: The authors have nothing to disclose.

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### Abstract

**Objectives:** To develop and validate a clinical diagnostic model based on optical pumped magnetometer magnetocardiography (OPM-MCG) for the detection of myocardial ischemia in patients with borderline coronary lesions prior to invasive coronary angiography (CAG).

Design: Prospective observational cohort study.

Setting: Single center of the China National Clinical Research Center for Cardiovascular Disease (NCCMRC).

Participants: Adults with borderline coronary lesions on CAG (N=141).

Interventions: Underwent OPM-MCG before CAG and fractional flow reserve (FFR) measurement.

**Results:** Five parameters were included in the final diagnostic model:  $MAg_{max}$ -TT,  $\delta Dt_{sum}$ -PN,  $\delta Ag_{sum}$ -C,  $\delta Ar_{sum}$ -N and  $\delta Ar_{min}$ -N. 1000 bootstrap replications showed that the area under the receiver operating characteristic curve (AUC) and 95% confidence interval (CI) of the diagnostic model were 0.864 (0.803-0.925), with sensitivity of 79.4%, specificity of 80.8%, positive predictive value of 79.4%, negative predictive value of 80.8%. Decision curve analysis showed a net benefit from the predictive model when the threshold probability of an ischemic patient was greater than 12%, suggesting the potential utility of the model in the real world.

**Conclusions:** A nomogram based on five OPM-MCG parameters was developed to assess myocardial ischemia in patients with borderline coronary lesions and has the potential to reduce the need for unnecessary CAG.

Trial registration number: ChiCTR2300072382.

 **Keywords:** borderline coronary lesions; optical pumped magnetometer magnetocardiography; fractional flow reserve; myocardial ischemia

# Strengths and limitations of this study

1) As a prospective observational cohort study, this study provides real-world evidence of the diagnostic performance of OPM-MCG for myocardial ischemia, enhancing the generalization of the findings.

2) The study was a single-center study, which may affect its adaptability to different settings. 3) The clinical diagnostic model did not account for myocardial ischemia due to coronary microcirculatory dysfunction and did not include evaluations performed with other magnetocardiography devices. erie

#### Introduction

Borderline coronary lesions exhibit ranging from 40% to 90% as seen in invasive coronary angiography (CAG). The FAME study ^[1] found that over 80% of lesions fell into this category, with only 35% of stenoses between 50-70% being hemodynamically significant. Predicting relevance was most accurate when estimating coronary artery diameter over 90%. Therefore, fractional flow reserve (FFR) guided intervention in patients with borderline coronary lesions (40-90% stenosis) has become a recommended treatment strategy in the 2018 ESC Interventional Guidelines ^{[2].} The 2021 ACC/AHA/SCAI Guidelines for Coronary Artery Revascularization ^[3] also provide clear recommendations for managing borderline coronary lesions: FFR and instantaneous wave-free ratio (iFR) are used to assess the need for percutaneous coronary intervention (PCI) in patients without evidence of ischemia but with angina and other equivalent symptoms (Class I); PCI is not recommended for stable patients with FFR >0.8 or iFR >0.89 (Class III). However, its widespread adoption in coronary catheter laboratories is hindered by its time-consuming nature, resource consumption, and potential adverse effects associated with adenosine application.

Optical pumped magnetometer magnetocardiography (OPM-MCG) measures tiny magnetic fields (10⁻¹⁵ Tesla) from the heart using atomic magnetometer technology, without radiation. It is quick, contactless, and suitable for diverse populations. Clinical studies have demonstrated that magnetocardiography (MCG) is superior to electrocardiogram (ECG) in detecting early myocardial ischemia ^[4,5,6,7] and has similar diagnostic effectiveness as SPECT for coronary artery disease (CAD) ^[8,9]. MCG was proven to be precise in diagnosing non-ST-segment elevation myocardial infarction, even in individuals who do not exhibit typical angina symptoms. ^[10,11]. However, the parameters and cut-off values of OPM-MCG that indicate myocardial ischemia in borderline coronary lesion are presently undefined.

Hence, this study aims to investigate the accuracy of OPM-MCG in diagnosing myocardial ischemia in patients with borderline coronary lesions, with invasive FFR measurement serving as the reference standard.

#### Method

#### **Study population**

This study was a prospective, single-center, observational, cohort study which was reviewed by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University, Page 7 of 41

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and registered with the China Clinical Trial Registry (ChiCTR2300072382). All participants signed an informed consent. The methods described in this article follow the STARD 2015 guidelines.

Participants aged 18-80 with typical angina symptoms (CCS class II or higher) or 40-90% stenosis on CCTA were scheduled for hospitalization for CAG. Exclusion criteria included: 1) Coronary artery stenosis outside of 40%-90% range on CAG; 2) Acute myocardial infarction; 3) Previous myocardial infarction; 4) Complex arrhythmias; 5) Bundle-branch block; 6) Pacemakers, metallic implants in trunk; 7) Claustrophobia.

This study was based on a prospective cohort design, the sample size of which was calculated by PASS 2021 software using the area under the receiver-operating characteristic (ROC) curve. The significance level ( $\alpha$ ) was 0.025 and the degree of certainty (1- $\beta$ ) was 0.90, combining the results of the literature review of related studies as well as the statistics of the small sample in the previous period, and calculating according to the FFR-positive (ischemic)/FFR-negative (non-ischemic) =2:3. The sample size was calculated as 138.

A total of 163 patients from June 30th to November 30th, 2023 were consecutively enrolled, and 22 patients were excluded, of which 11 patients with stenosis >90%, 7 patients underwent direct PCI without FFR testing, and 4 patients with poor quality MCG imaging, and Finally 141 patients with borderline coronary lesions underwent MCG and FFR sequentially (Figure 1). In this study, the cardiologists were not aware of the MCG results at the time of the FFR examination, and the MCG parameters were determined before the FFR examination (Supplementary Figure 1-Graphical Abstract).

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# CAG and FFR procedures

CAG and FFR measurements were performed on the vessels according to the 2021 ACC/AHA/SCAI Guidelines for Coronary Artery Revascularization and Expert consensus on the clinical pathway for FFR measurement in China. After administration of nitroglycerin, a pressure monitoring guidewire was advanced through the stenosis. Hyperemia was attained by administration of intravenous adenosine ( $140\mu g/kg/min$ ). The FFR pressure wire was positioned a minimum of 20 mm distal to the stenosis in vessel segments  $\geq 2$  mm. The presence of an FFR  $\leq 0.80$  was considered a positive indicator of functional ischemia in patients and was defined as the FFR-positive group.

## MCG imaging

The MCG recordings were conducted using a 36-channel OPM-MCG system (Miracle MCG), featuring OPM sensors sourced from Beijing X-Mag Technologies Limited's mature commercial product. The OPM sensor is based on spin-exchange relaxation free (SERF) technology, with alkali metal atoms as the core sensitive element. The OPM sensor has a sensitivity below 30 fT/Hz^{1/2}, a recording bandwidth of 1 Hz to 40 Hz, a sampling frequency of 200 Hz, and a noise baseline with not higher than 15 fT. The OPM-MCG residual magnetic field is kept below 1.5 nT, and the data acquisition mode is analog signal acquisition (Supplementary Figure 2). Each subject had a 90-second continuous recording at 36 locations ( $6 \times 6$  grid) above the chest using an arrayed sensor grid.

## MCG Signal Analysis and Statistical Analysis

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After MCG data acquisition, the software automatically post-processes the signals to generate magnetic field and current density maps and output sixty-five parameters (Supplementary Table 1). The sixty-five parameters we output characterize the stability of the current dipole in the TT segment (the position from one-third of the T max amplitude (T onset) to T max (T peak)) according to the previous studies of Park et al. and Pena et al. (see supplementary material for post-processing steps).

Statistical analysis was performed with SPSS 25.0 and R 4.3.2 (http://www.R-project.org/). Counting data were presented as numbers and percentages, while normally distributed measurement data were shown as mean  $\pm$  standard deviation. Continuous variables that were not normally distributed were presented using median and quartile values. Statistical significance was determined for all analyses with a P-value less than 0.05. Based on this cohort and the principle of at least 10 events per variable (10 EPV), we considered the rationality of the parameters included in the diagnostic model and evaluated the number of parameters. sixtyfive potential predictor variables were evaluated using univariable logistic regression, selecting those with p-values  $\leq 0.1$ . These variables were then subjected to Least Absolute Shrinkage and Selection Operator (LASSO) regression, ultimately identifying the most impactful predictors. Continuous variables representing the amount of change were transformed into ordered categorical variables based on interquartile range. Continuous variables representing absolute values were converted into dichotomous variables by grouping their upper and lower quartile values into extreme categories, while middle-range values were grouped and incorporated into the model. The final model was developed using multivariate logistic regression with a backward selection approach. The model's predictive performance was assessed using the

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enhanced bootstrap method and clinical benefit was evaluated using decision curve analysis. The nomogram was used to report scores for assessing myocardial ischemia with OPM-MCG parameters.

# **Patient and Public Involvement**

Patients make more people aware of the clinical use of the OPM-MCG and how it is examined by sharing news and information about clinical studies with others.

#### Result

#### **Clinical characteristics**

The study included 141 patients, mostly male (77.3%) with an average age of  $60.64 \pm 9.70$  years. After MCG scans, all patients underwent CAG and FFR examination, with 48.2% having positive FFR (FFR  $\leq 0.8$ ). A total of 157 vessels were examined, with 47.1% having FFR  $\leq 0.8$ . Interval between MCG and FFR less than 30 days, median 2 days. Most patients had FFR measurements primarily done on the left anterior descending artery. See Table 1 for patient clinical characteristics.

#### Selection of parameters and development of the diagnostic model

Fifty variables that were statistically significant (P < 0.1) in univariable logistic regression were included in the LASSO regression (Supplementary Table 2 and Supplementary Figure 3), and 8 variables were selected based on the reasonableness of the parameters selected to reduce the model overfitting and covariance through LASSO regression. By using the backward

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approach, 5 parameters were included in the final diagnostic model:  $MAg_{max}$ -TT,  $\delta Dt_{sum}$ -PN,  $\delta Ag_{sum}$ -C,  $\delta Ar_{sum}$ -N and  $\delta Ar_{min}$ -N (Table 2, Figure 2). The model area under the receiver operating characteristic curve (AUC) obtained from multivariate logistic regression analysis was 0.864, with sensitivity of 79.4%, specificity of 80.8%, positive predictive value of 79.4%, negative predictive value of 80.8% (See Supplementary Figure 4 for the confusion matrix of the diagnostic model). The nomogram (Figure 3) provides a graphical overview of the diagnostic model using multivariate logistic regression analysis (Supplementary Table 3).

# Internal validation and net benefit of the model

The model performance for the diagnosis of myocardial ischemia in borderline coronary lesions of the OPM-MCG was evaluated by bootstrap replications. 1000 bootstrap replications showed that the model AUC and a 95% confidence interval (CI) of 0.864(0.803-0.925) (Figure 4). 1000 bootstrap replications showed that the mean absolute error was 0.017 (Figure 4). The decision curve analysis (DCA) for the diagnostic model showed that if the threshold probability of patients is greater than 12% (Figure 4), screening strategies based on the OPM-MCG diagnostic model resulted in superior net benefit than screen-none or screen-all strategies. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

# Discussion

CAD is presently characterized by an epicardial vascular lesion with a stenosis exceeding 50% in the CAG. Frequently, the degree of stenosis indicated by CAG is used as a reference standard for myocardial revascularization. Moreover, FFR can be used to evaluate the existence of myocardial ischemia, with a threshold of 0.8. However, as illustrated in Figure 2, the

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coronary stenosis identified in CAG may not precisely align with the FFR results. This observation is in line with the conclusions drawn in the 2019 ESC Guidelines for Chronic Coronary Syndromes ^[12,13], emphasizing that the accuracy of determining CAD solely based on angiographic stenosis was as low as 64% when compared to flow reserve fraction. The positive mismatch rate, where lesions with less than 50% stenosis may demonstrate an FFR  $\leq 0.8$ , was 19%, while the negative mismatch rate, where lesions with over 50% stenosis may result in an FFR value > 0.8, reached up to one-third. Numerous studies ^[14,15] have consistently demonstrated that FFR-guided stenting leads to superior immediate outcomes and long-term prognosis. Therefore, FFR carries a Class 1a recommendation for guiding revascularization in angiographically borderline coronary stenoses in patients with stable angina. The feasibility of diagnosing myocardial ischemia in patients with borderline coronary lesions using OPM-MCG was shown in our study, when compared to invasive FFR. The collective diagnostic potential of MCG parameters in detecting myocardial ischemia in borderline coronary lesions resulted in an AUC of 0.864 (95% CI 0.803 to 0.925). Due to factors such as time consumption, costs, patient-related discomfort, contraindications, and a lack of reimbursement, the current rate of FFR utilization in catheterization laboratories in China is less than 6% ^[3]. OPM-MCG allows ischemia assessment in patients with borderline coronary lesions prior to CAG and has a good concordance with FFR.

In comparing our MCG results with those reported by Park JW et al. ^[16], it is clear that FFR, serving as the reference standard, evaluates ischemia through direct measurement of pressure beyond the coronary lesion. In contrast, the Five parameters of our OPM-MCG, along with the ST-segment fluctuation scores (AUC=0.835) and Bull's eye analysis (AUC=0.914)

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employed by Park, offer a non-invasive alternative. According to Park JW et al, the TT segment, defined as the interval from T onset to T peak, is a more effective parameter for analyzing MCG signals due to its superior signal-to-noise ratio for reflecting ventricular repolarization electrical activity ^[17]. In terms of the selected parameters, consistent with earlier literature ^[18], we focused on assessing the overall homogeneity of the repolarization process, including spatial structural similarity and smoothing of current changes. Park et al. utilized ST-segment fluctuation scores and Bull's eye analysis to evaluate the uniformity of the repolarization process in relation to current variations and spatial distribution variances for ischemia assessment. In our study, we further characterized the images by incorporating the  $\delta Dt_{sum}$ -PN,  $\delta Ag_{sum}$ -C,  $\delta Ar_{sum}$ -N and  $\delta$ Ar_{min}-N parameters of the model to analyze changes in currents, pole areas, and distances. Additionally, describing the images using the parameters of the 3 different angular points provided a comprehensive description and response to the images. In terms of image feature discrimination, the ischemia-positive features of the OPM-MCG (pole multipolarization and magnetic field angle deflection) initially are consistent with the FFR (Figure 2). For practical clinical application, Park JW et al. used a 64-channel axial gradiometer system, which offers greater channel capacity and higher sensitivity for positional discrimination. However, this approach required patients to complete two MCG tests-one during stress and one at rest-in a shielded room. Comparatively, OPM-MCG is equipped with a shielding barrel that can effectively diagnose myocardial ischemia caused by borderline coronary lesions at rest, without the need for a specially constructed shielding room. This enhances the practicality and universality of its clinical application.

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Non-invasive methods like positron emission tomography / computed tomography

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(PET/CT), single-photon emission computed tomography (SPECT) and cardiovascular magnetic resonance (CMR) are accurate for assessing myocardial ischemia, but their use is limited due to cost, long wait times and radioactive substances ^[19]. In a prospective study done by Roel S. et al. ^[20], which included 189 patients in a head-to-head comparison, it was found that using FFR as the gold standard, the sensitivity of SPECT, PET/CT, and CMR was only 67%, 81%, and 66%, and the specificity was only 61%, 65%, and 62%. The diagnostic accuracy of PET/CT was not statistically different from that of SPECT and CMR. Recently, CT-derived fractional flow reserve (CT-FFR) has emerged as a noninvasive test for detecting myocardial ischemia, with a sensitivity of 89% and specificity of 91% according to a multicenter study [21]. The widespread use of CT-FFR has limitations including the need for good image quality and inability to assess microvascular and diffuse lesions ^[22]. ECG is widely used in the clinic as the fastest and low-cost test. ECG uses a two-dimensional linear approach to record cardiac radial currents to detect ischemia, but it can be affected by body tissues or fluids and has low spatial resolution. MCG detects and measures weak magnetic fields generated by the electrical activity of the heart, and the waveform of the MCG waveform is similar to that of the ECG signal. However, MCG is less affected by changes in conductivity and does not suffer from skin electrode contact problems. In addition, MCG is more sensitive to magnetic fields generated by tangential currents that are more affected by myocardial ischemia, and MCG detects eddy currents that are not apparent with ECG [23]. Thus, previous studies have demonstrated that MCG has a higher sensitivity to early myocardial ischemia ^[24,25]. In most studies of MCG detection of myocardial ischemia, researchers have categorized the analysis of MCG into morphological and quantitative data analyses ^[26]. Morphological analysis often focuses on

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amplitude, nondipole phenomena, and current or magnetic field angle. Quantitative data analysis is mostly based on changes in the magnetic field during ventricular repolarization, usually at the end of the ST segment (before the T wave) and/or during the T wave, and partially measured during the QT and QRS segment. These parameters describe the poles, the angles of the magnetic and current fields, and the waveform amplitude by extrema, dynamics, and ratios. Current studies analyzing MCG at rest for the detection of myocardial ischemia use a variety of methods, including dichotomous classification methods based on MCG parameters, quantification of abnormal MCG parameters, creation of composite indices using MCG parameters, and the application of machine-learning methods ^[27].

This is similar to our finding that a positive OPM-MCG scan was demonstrated by one or more abnormalities in the TT segment, including changes in TT segment parameters and the changes in image (non-dipole phenomena and angular deflection of currents or magnetic fields). Different MCG parameters and their combinations can provide more incremental information on cardiovascular disease. In addition, studies have shown that MCG is capable of accurately diagnosing myocardial ischemia resulting from epicardial coronary artery disease as well as effectively detecting myocardial ischemia caused by coronary microvascular dysfunction (CMD). The accuracy of MCG identification of CMD is 94.8%, sensitivity of 100%, and specificity of 93.3% ^[28]. In our study, we also found a small number of FFR-negative patients with positive MCG scans as described above, and considered the possibility of CMD. In the future, we will summarize the characteristic images of patients with CMD and further explore the incremental information provided by the MCGs for these patients.

The difference between SQUID-based and OPM-based MCG systems lies on their sensor

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technology. SQUID-based MCGs were developed earlier and offer high sensitivity. But their reliance on liquid helium refrigeration for achieving low-temperature superconductivity, as well as the high maintenance costs associated with them, have hindered their widespread adoption and utilization. In contrast, the OPM-MCG operates at room temperature without liquid helium cooling and offers comparable sensitivity, as it is easier to use and less expensive to operate ^[29,30]. However, OPM-MCG is also unsuitable for claustrophobic patients. Furthermore, as a result of its late development, there is a lack of established guidelines for analyzing MCG parameters. As such, we intend to conduct further exploratory studies on OPM-MCG in various clinical settings.

#### Limitation

The study is a single-center registry study with some limitations. We are aware that the current diagnostic model may suffer from potential overfitting and therefore the conclusions of this study require further validation in multicenter studies. In addition, the definition of positive and negative poles we currently use differs from the Rome Biomag Conference in 1981 standard, and there are currently multiple types of MCGs globally, and the current methodology for analyzing myocardial ischemia has not been compared head-to-head with other MCG devices.

# Conclusion

MCG shows excellent sensitivity, specificity, and diagnostic accuracy in identifying significant myocardial ischemia when compared to FFR. MCG can provide the evidence of a

 precise diagnostic strategy in patients with borderline coronary lesions before CAG, reducing unnecessary invasive examination.

# Ethics approval and consent to participate

This study was performed in accordance with the principles of the Declaration of Helsinki. This study was approved by the ethics committee of Beijing Anzhen Hospital, Capital Medical University (KS2023008). Written informed consent was required for participation in the study.

# **Competing interests**

The authors declare that they have no conflicts of interest.

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#### **Author Contribution Statement**

Xiantao Song and Chenchen Tu acted as guarantors. Xiantao Song, Chenchen Tu and
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Hongjia Zhang helped to conceive the topic and revised the article. Shuwen Yang and Lanxin Feng wrote the manuscript and finished the statistics, Mingduo Zhang, Min Zhang, Jiqiang He, Yanlong Ren, Yawei Luo and Feng Xu contributed to the data collection. Zhao Ma, Huan Zhang, Yazhe Zhang, Linqi Liu, Shu Zhou, Xin Zhao, and Xueyao Yang helped with data analysis. All authors read and approved the final manuscript.

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#### Abbreviations

AUC= area under the receiver operating characteristic curve

CAD= coronary artery disease

CAG= coronary angiography

CCTA= coronary computed tomography angiography

CI= confidence intervals

CMR= cardiovascular magnetic resonance

CT-FFR= CT-derived fractional flow reserve

ECG= electrocardiogram

FFR= fractional flow reserve

iFR=instantaneous wave-free ratio

LASSO= Least Absolute Shrinkage and Selection Operator

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- MCG= magnetocardiography
- OPM-MCG= optical pumped magnetometer magnetocardiography
- PCI= percutaneous coronary intervention
- PET/CT= positron emission tomography / computed tomography
- ROC= receiver-operating characteristic
- SPECT= single-photon emission computed tomography

## Availability of data and materials

The data that support the findings of this study are available on request from the corresponding author, Xiantao Song, upon reasonable request.

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Table 1 Clinical characteristics (n = 141)

Characteristics	Total(n=141)			
Age (yrs)	60.64±9.70			
Male, n (%)	109(77.3)			
BMI (Kg/m2)	26.15±3.36			
Diabetes, n (%)	47(33.3)			
Hypercholesterolemia, n (%)	65(46.1)			
Hypertension, n (%)	82(58.2)			

Stroke, n (%)	9(6.4)
Smoke, n (%)	43(30.5)
Systolic blood pressure, mmHg	128.69±15.54
Diastolic blood pressure, mmHg	75.15±10.79
Heart rate	73.81±10.38
Medication, n(%)	
Aspirin	129(91.5)
Statin	137(97.2)
ACEI/ARB	45(35.6)
SGLT2 inhibitors	22(16.7)
Nicorandil	23(16.3)
Admission lab results	
Low-density lipoprotein cholesterol (mmol/L)	1.82±0.69
hs Tnl(pg/ml)	3.5(2.5,5.8)
Brain natriuretic peptide (pg/ml)	29.00(14.75,48.25)
Blood glucose (mmol/L)	5.52(4.82,7.33)
HbA1c(%)	6.25(5.7,7.1)
ICA and FFR characteristics	
1-vessel disease	50(35.5)
2-vessel disease	43(30.5)
3-vessel disease	48(34.0)

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Number of patients with FFR $\leq 0.8$	68(48.2)
Number of vessels with FFR	157
Number of vessels with FFR $\leq 0.8$	74(47.1)
Left anterior descending artery with FFR	97(68.8)
Left circumflex artery with FFR	25(17.7)
Right coronary artery with FFR	35(24.8)
Interval between MCG and FFR	2(1,7)

Values are n (%) or mean  $\pm$  SD

BMI= Body Mass Index, ACEI= angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker, SGLT2 inhibitors = sodium-glucose cotransporter-2 inhibitors, HbA1c= glycated hemoglobin, ICA = invasive coronary angiography, FFR = fractional flow reserve.

## Table 2 The definitions of the MCG parameters

MCG Parameters	Definitions
MAg _{max} -TT	The maximum magnetic field angle at intervals of a certain time $\tau$
	within TT segment
δDt -PN	The sum of changes in magnetic pole distance at intervals of a
	certain time $\tau$ within TT segment
δλα Γ	The sum of changes in current angle at intervals of a certain time $\boldsymbol{\tau}$
on g _{sum} -C	within TT segment
$\delta Ar_{sum}$ -N	The sum of changes in negative pole area at intervals of a certain

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 M= Magnetic Field; Ag= Angle; TT= from T onset to T peak; δ= Change value; DT= Distance;

 PN= Positive Pole to Negative Pole; C=Current; Ar= Area; N= Negative Pole; ; τ= one tenth

 of the time interval between TT segment.

 Figure legend

 Figure 1. Flowchart of the study design.

 Figure legend: CCTA= coronary computed tomography angiography;

 MCG=magnetocardiography; ICA= invasive coronary angiography; FFR=fractional flow

reserve; PCI= percutaneous coronary intervention.

Figure 2 Schematic diagram of OPM-MCG scan.

Figure legend: (A) Schematic diagram of MAg_{max}-TT and current angle. In magnetic field distribution maps and current density maps, the definition rule for angle values is based on the horizontal axis, with counterclockwise angles being negative and clockwise angles being positive. MAg_{max}-TT is the maximum angle between the line connecting the maximum positive and negative magnetic poles and the horizontal axis. in the TT segment.  $\delta$ Ag_{sum}-C is the sum of changes in current angle at intervals of a certain time  $\tau$  within TT segment (B)Normal OPM-MCG scan. The OPM-MCG scan showed no evidence of ischemia or obstructive coronary artery disease, as demonstrated by the lack of significant current Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

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deviations within the myocardium and absence of angle shift between the positive red pole and negative blue pole between T-onset and T-peak. (C) The OPM-MCG scan of a patient in his 70s showed magnetic field angular deflection, abnormal magnetic field distribution of the positive and multipolarisation of negative poles, suggesting significant myocardial ischemia, and the ECG showed no significant abnormality. The CAG showed two lesions: 60% stenosis of the D1, 50% stenosis of the R-PDA. The FFRs were 0.77 for the R-PDA. (D) The OPM-MCG scan of a patient in his 60s showed no myocardial ischemia, ECG showed no significant abnormalities, echocardiography showed widening of the ascending aorta and aortic sinus. CAG showed 75% stenosis of the LAD, 60% stenosis of the RCA, FFR value of the LAD was 0.88.

MCG= magnetocardiography; FFR= fractional flow reserve; ICA= invasive coronary angiography; D1= diagonal branches; R-PDA= posterior descending artery; LAD= left anterior descending artery; RCA= right coronary artery.

Figure 3. Nomogram of the diagnostic model.

Figure legend: The nomogram graphically demonstrates the diagnostic model of OPM-MCG. Points for MAg_{max}-TT,  $\delta Dt_{sum}$ -PN,  $\delta Ag_{sum}$ -C,  $\delta Ar_{sum}$ -N and  $\delta Ar_{min}$ -N can be obtained using a point caliper and then summed to obtain a total score that can be measured with diagnosing myocardial ischemia in patients with borderline coronary lesions.

Figure 4 Accuracy and internal validation of the diagnostic model.

Figure legend: (A) ROC curves for the diagnostic model. After 1000 bootstrap replications, the

area under the curve and 95% confidence interval for receiver operating characteristic is 0.864 (0.803-0.925). (B) Calibration curve for the diagnostic model. Calibration curve for the borderline lesion ischemia diagnostic model was established by comparing the actual and predicted probability of a positive FFR in patients with borderline lesions of the coronary arteries. The smaller the distance of the scatter from the dashed line, the better the calibration. (C) Decision curve analysis (DCA) for diagnostic models of ischemia in borderline coronary lesions. Treat none: net benefit when it is assumed that no patients with borderline lesions of the coronary arteries would have the outcome (FFR-positive). Treat all: net benefit when all patients with borderline coronary lesions are assumed to have an outcome (FFR-positive). Diagnostic model: net benefit of managing borderline coronary lesions with a diagnosis of myocardial ischemia based on the diagnostic model estimate. The strategy with the highest net benefit at any given threshold is the preferred strategy.

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Figure legend: CCTA= coronary computed tomography angiography; MCG=magnetocardiography; ICA= invasive coronary angiography; FFR=fractional flow reserve; PCI= percutaneous coronary intervention.

510x441mm (96 x 96 DPI)



#### Figure 2 Schematic diagram of OPM-MCG scan.

Figure legend: (A) Schematic diagram of MAgmax-TT and current angle. In magnetic field distribution maps and current density maps, the definition rule for angle values is based on the horizontal axis, with counterclockwise angles being negative and clockwise angles being positive. MAgmax-TT is the maximum angle between the line connecting the maximum positive and negative magnetic poles and the horizontal axis. in the TT segment. δAgsum-C is the sum of changes in current angle at intervals of a certain time τ within TT segment (B)Normal OPM-MCG scan. The OPM-MCG scan showed no evidence of ischemia or obstructive coronary artery disease, as demonstrated by the lack of significant current deviations within the myocardium and absence of angle shift between the positive red pole and negative blue pole between T-onset and T-peak. (C) The OPM-MCG scan of a patient in his 70s showed magnetic field angular deflection, abnormal magnetic field distribution of the positive and multipolarisation of negative poles, suggesting significant myocardial ischemia, and the ECG showed no significant abnormality. The CAG showed two lesions: 60% stenosis of the D1, 50% stenosis of the R-PDA. The FFRs were 0.77 for the R-PDA. (D) The OPM-MCG scan of a patient in his 60s showed no myocardial ischemia, ECG showed no significant abnormalities, echocardiography showed widening of the ascending aorta and aortic sinus. CAG showed 75% stenosis of the LAD, 60% stenosis of the RCA, FFR value of the LAD was 0.88.

MCG= magnetocardiography; FFR= fractional flow reserve; ICA= invasive coronary angiography; D1=

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Diagonal branches; R-PDA= Posterior descending artery; LAD= Left Anterior descending artery; RCA= right coronary artery.

1090x1206mm (96 x 96 DPI)



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#### Figure 4 Accuracy and internal validation of the diagnostic model.

Figure legend: (A) ROC curves for the diagnostic model. After 1000 bootstrap replications, the area under the curve and 95% confidence interval for receiver operating characteristic is 0.864 (0.803-0.925). (B) Calibration curve for the diagnostic model. Calibration curve for the borderline lesion ischemia diagnostic model was established by comparing the actual and predicted probability of a positive FFR in patients with borderline lesions of the coronary arteries. The smaller the distance of the scatter from the dashed line, the better the calibration. (C) Decision curve analysis (DCA) for diagnostic models of ischemia in borderline coronary lesions. Treat none: net benefit when it is assumed that no patients with borderline lesions of the coronary arteries would have the outcome (FFR-positive). Treat all: net benefit when all patients with borderline coronary lesions are assumed to have an outcome (FFR-positive). Diagnostic model: net benefit of managing borderline coronary lesions with a diagnosis of myocardial ischemia based on the diagnostic model estimate. The strategy with the highest net benefit at any given threshold is the preferred strategy.

239x257mm (375 x 375 DPI)

# **Supplementary Material**

Development and validation of a clinical diagnostic model for myocardial ischemia in borderline coronary lesions based on optical pumped magnetometer magnetocardiography: a prospective observational cohort study

## Contents

Development and validation of a clinical diagnostic model for myocardial ischemia in borderline
coronary lesions based on optical pumped magnetometer magnetocardiography: a prospective
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Coronary Artery Lesions

## **Optical pumped magnetometer magnetocardiography (OPM-MCG) post-processing steps**

BMJ Open tical pumped magnetometer magnetocardiography (OPM-MCG) post-processing steps The post-processing process of OPM-MCG signals is as follows. Firstly, a composite gradient magnetometer agrees a structed using a separate environmental monitoring channel, and the common mode projection components of the monitoring channel are subtracted from the OPM-MCG detection array channels, effectively suppressing environmental magnetic field drift and power frequency and its harmonic components of the data, and performing a 1-40Hz bandpass filter to will be remove power frequency the Sditz power frequency and its harmonic components of the data, and performing a 1-4042 bandpass filter to the main frequency range of the MCG. Finally, the denoised data and prover the data and overlay it for average and the slice time, and the identified alignment point to slice the data and overlay it for average. interference and limit the bandpass frequency to the main frequency range of the MCG. Finally, the denoised data spectral to R-peak detection





Supplementary Figure 1 Graphical Abstracts: Diagnostic Model of Myocardial Ischemia in Borderline Coronard Artery Lesions Based on **OPM-MCG** 

CCTA= coronary computed tomography angiography; OPM-MCG=optical pumped magnetometer magnetocardiography; CAG= invasive coronary angiography; FFR=fractional flow reserve; PCI= percutaneous coronary intervention; DCA=decision curve analysis. liographique de l





converge, and there are fewer parameters with non-zero regression coefficients.(B) Tuning parameter selection by cress-validation in the LASSO model. The solid vertical lines represent the partial likelihood deviance standard error (SE). The red dotted line indicates the cross-validation curve. The vertical dashed lines are drawn at the optimal values on the basis of the minimum criteria and 1-SE criteria. Considering the reasonableness of the variables included in this model, with the  $\lambda$  value of 0.02380779 was chosen. liographique de l



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	Sunnlementary 7	Fable 1 OPM-MCG Parameters and Definitions
	Parameters	Definition
	δ Ag _{max} -M	The maximum value of changes in magnetic field angle at intervals of a certain time $\tau$ with $\frac{1}{3}$ T B segment
	δ Ag _{min} -M	The minimum value of changes in magnetic field angle at intervals of a certain time $\tau$ within Tresegment
	$\delta \mathbf{A} \mathbf{g}_{std} - \mathbf{M}$	The standard deviation of changes in magnetic field angle at intervals of a certain time $\tau$ within $T$ segment
	δ Ag _{sum} -M	The sum of changes in magnetic field angle at intervals of a certain time $\tau$ within TT segments
	δ Dt _{max} -PN	The maximum value of changes in magnetic pole distance at intervals of a certain time $\tau$ with $\beta$ T segment
	$\delta Dt_{min}$ -PN	The minimum value of changes in magnetic pole distance at intervals of a certain time $\tau$ with $\vec{h}$ T segment
	$\delta \mathbf{D} \mathbf{t}_{\text{std}} - \mathbf{P} \mathbf{N}$	The standard deviation of changes in magnetic pole distance at intervals of a certain time $\tau$ with TT segment
	$\delta \mathbf{D} \mathbf{t}_{sum}$ -PN	The sum of changes in magnetic pole distance at intervals of a certain time $\tau$ within TT segures to
	$\delta Ag_{max}$ -C	The maximum value of changes in current angle at intervals of a certain time $\tau$ within TT some that
	δ Ag _{min} -C	The minimum value of changes in current angle at intervals of a certain time $\tau$ within TT setting at
	$\delta Ag_{std}$ -C	The standard deviation of changes in current angle at intervals of a certain time $\tau$ within TT $\overline{\mathbf{x}}$ within TT
	$\delta A \sigma_{sum}$ -C	The sum of changes in current angle at intervals of a certain time $\tau$ within TT segment
	δ Psmax-C	The maximum value of changes in the position of the current angle at intervals of a certain time within TT segment
	$\delta \mathbf{P}_{\mathbf{S}_{\mathbf{s}td}}$ -C	The standard deviation of changes in the position of the current angle at intervals of a certain $t \vec{\mathbf{x}}$ within TT segment
	δ Pssum-C	The sum of changes in the position of the current angle at intervals of a certain time $\tau$ within TT segment
	$\delta Ar_{max}$ -NP	The maximum value of changes in negative pole point area at intervals of a certain time $\tau$ within TT segment
	$\delta A \mathbf{r}_{min}$ -NP	The minimum value of changes in negative pole point area at intervals of a certain time $\tau$ within TT segment
	$\delta \mathbf{Ar}_{\text{ord}} - \mathbf{NP}$	The standard deviation of changes in negative pole point area at intervals of a certain time <b>T</b> segment
	$\delta \mathbf{Ar}_{\text{sum}}$ -NP	The sum of changes in negative pole point area at intervals of a certain time. The within TT segment
	$\delta A r_{\rm hm}$ -NP	The change in negative pole point area between T-begin and T-neak
	$\Delta r_{max}$ -NP	The maximum value of the negative pole point area at intervals of a certain time $\tau$ within T $\mathbf{p}$ second
	$Ar_{min}$ -NP	The minimum value of the negative pole point area at intervals of a certain time $\tau$ within These terms of the negative pole point area at intervals of a certain time $\tau$ within These terms of the negative pole point area at intervals of a certain time $\tau$ within These terms of the negative pole point area at intervals of a certain time $\tau$ within These terms of the negative pole point area at intervals of a certain time $\tau$ within These terms of the negative pole point area at intervals of the negative pole pole point area at intervals of the negative pole pole pole pole pole pole pole pol
	δ Ps _{max} -NP	The maximum value of changes in the position of the negative pole point at intervals of a central time $\tau$ within TT segment
	$\delta \mathbf{P}_{\mathbf{S}_{\mathbf{s}\mathbf{t}\mathbf{d}}}\mathbf{N}\mathbf{P}$	The standard deviation of changes in the negative of the positive pole point at intervals of a central time $\tau$ within TT segment
	δ Ps _{sum} -NP	The sum of changes in the position of the negative pole point at intervals of a certain time $\tau$ with $\mathbf{F}$ TT segment
	δ Ar _{max} -N	The maximum value of changes in negative pole area at intervals of a certain time $\tau$ within TT suggement
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Parameters	Definition
δ Ag _{max} -M	The maximum value of changes in magnetic field angle at intervals of a certain time $\tau$ with $\frac{2}{3}$ T is segment
$\delta Ar_{min}$ -N	The minimum value of changes in negative pole area at intervals of a certain time $\tau$ within $\exists t$ segment
$\delta$ Ar _{std} -N	The standard deviation of changes in negative pole area at intervals of a certain time $\tau$ with $\mathbf{\vec{g}}$ T resegnent
δ Ar _{sum} -N	The sum of changes in negative pole area at intervals of a certain time $\tau$ within TT segment $\frac{1}{5}$
δ Ar _{bp} -N	The change in nagative pole area between T-begin and T-peak
Ar _{max} -N	The maximum value of the negative pole area at intervals of a certain time $\tau$ within TT segments
Ar _{min} -N	The minimum value of the negative pole area at intervals of a certain time $\tau$ within TT segner $\mathbf{z}$
δ ArRto _{max} -PN	The maximum value of changes in the ratio of positive and negative pole area at intervals of $\vec{r}$ tain time $\tau$ within TT segment
δ ArRto _{min} -PN	The minimum value of changes in the ratio of positive and negative pole area at intervals of $\frac{3}{2}$ tain time $\tau$ within TT segment
$\delta$ ArRto _{std} -PN	The standard deviation of changes in the ratio of positive and negative pole area at intervals of $\vec{p}$ segment $\tau$ within TT
δ ArRto _{sum} -PN	The sum of changes in the ratio of positive and negative pole area at intervals of a certain time $\mathbf{\bar{z}}$ $\mathbf{\bar{z}}$ within TT segment
δ Ar _{max} -PP	The maximum value of changes in positive pole point area at intervals of a certain time 🔻 washing T segment
$\delta Ar_{min}$ -PP	The minimum value of changes in positive pole point area at intervals of a certain time $\tau$ within T segment
$\delta Ar_{std}$ -PP	The standard deviation of changes in positive pole point area at intervals of a certain time $\tau$ with TT segment
δ Ar _{sum} -PP	The sum of changes in positive pole point area at intervals of a certain time $\tau$ within TT segment
δ Ar _{bp} -PP	The change in positive pole point area between T-begin and T-peak
Ar _{max} -PP	The maximum value of the positive pole point area at intervals of a certain time $\tau$ within TT segment
Ar _{min} -PP	The minimum value of the positive pole point area at intervals of a certain time $\tau$ within TT $\beta$ egatent
δ Ps _{max} -PP	The maximum value of changes in the position of the positive pole point at intervals of $\vec{abcerea}$ in time $\tau$ within TT segment
$\delta Ps_{std}$ -PP	The standard deviation of changes in the position of the positive pole point at intervals of a $c_{g}$ train time $\tau$ within TT segment
$\delta \mathbf{Ps}_{sum}$ -PP	The sum of changes in the position of the positive pole point at intervals of a certain time $\tau$ with TT segment
δ Ar _{max} -P	The maximum value of changes in positive pole area at intervals of a certain time $\tau$ within TT s methods where the term of t
δ Ar _{min} -P	The minimum value of changes in positive pole area at intervals of a certain time $\tau$ within TT set ment
δ Ar _{std} -P	The standard deviation of changes in positive pole area at intervals of a certain time $\tau$ within T
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Parameters	Definition	
δ Ag _{max} -M	The maximum value of changes in magnetic field angle at intervals of a certain time <b>v</b> within the segment	
δ Ar _{sum} -P	The sum of changes in positive pole area at intervals of a certain time $\tau$ within TT segment $\frac{1}{2}$	
δ Ar _{bp} -P	The change in positive pole area between T-begin and T-peak	
Ar _{ma} x-P	The maximum value of the positive pole area at intervals of a certain time $\tau$ within TT segneration $\vec{r}$	
Ar _{min} -P	The minimum value of the positive pole area at intervals of a certain time $\tau$ within TT segment $\vec{a}$	
MAg _{max} -TT	The maximum magnetic field angle at intervals of a certain time $\tau$ within TT segment	
CAg _{max} -TT	The maximum current angle at intervals of a certain time $\tau$ within TT segment	
MAg _{min} -TT	The minimum magnetic field angle at intervals of a certain time $\tau$ within TT segment	
CAg _{min} -TT	The minimum current angle at intervals of a certain time $\tau$ within TT segment	
MAg-Rp	The magnetic field angle of the R-peak	
RtoAm-R _p T _p N	The ratio of magnetic field amplitude at R-peak and the negative amplitude at T-peak $\frac{1}{2}$	
RtoAm-R _p T _p P	The ratio o magnetic field amplitude at R-peak and the positive amplitude at T-peak	
RtoAm-R _p T _p	The ratio of magnetic field amplitudes at R-peak and T-peak	
MAg-RpTp	The magnetic field angle between R-peak and T-peak	
MAg-Tp	The magnetic field angle of the T-peak	
CAg _{max} -Tp	The maximum current angle at T-peak	
RtoAm-Tp	The ratio of positive to negative magnetic field amplitude at T-peak	
TT	The interval from the beginning of the T-wave to its peak within the cardiac cycle	
Dt = Distance, Ps Pole, M = Magne segment (the posi	= Position, $Ag = Angle$ , $Am = Magnitude$ , $Ar = Area$ , $Rto = Ratio$ , $P = Positive$ , $Positive Pole = IFP, N = Negative, NP tic Field, C = Current, max = Maximum, min = Minimum, sum=Sum of all, std = Standard deviation \delta = Change valution from one-third of the T max amplitude (T onset) to T max (T peak)), R_p=R peak, T_p=T peak$	= No 1e, T
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Supplementary Ta	able 2 OPM-MCG Paramet	ers of Univariable Logistic R	egression Model P < 0.1	24-086 ght, in	
Donomotona	ALL	FFR-Positive	FFR-Negative	Godds Ratio	Dualua
Parameters	N=141	N=68	N=73	ing (95%CI)	P value
δ Ag _{max} -M	0.62 (0.44,1.19)	0.77 (0.47,5.76)	0.54 (0.43,0.72)	<b>2</b> 1.0 <b>0</b> 7(1.023-1.163)	0.021
δ Ag _{min} -M	-0.34 (-0.57,-0.18)	-0.42 (-0.82,-0.28)	-0.26 (-0.42,-0.14)	kogy j 4(0.924-0.992)	0.034
δ Ag _{std} -M	0.16 (0.11,0.68)	0.28 (0.14,2.06)	0.14 (0.10,0.20)	<u>ē</u> 1594(1.213-2.313)	0.004
δ Ag _{sum} -M	10.6 (6.18,26.2)	20.2 (9.88,45.5)	8.28 (4.55,11.8)	at e. §64(1.037-1.1)	< 0.001
δ Dt _{max} -PN	2.69 (1.97,4.12)	3.51 (2.16,12.9)	2.22 (1.89,3.16)	ອີເຊັ່ງອີຊີ4(1.001-1.032)	0.063
$\delta Dt_{min}$ -PN	-2.20 (-3.27,-1.76)	-2.38 (-4.70,-1.91)	-2.00 (-2.80,-1.63)	<b>2 2</b> 1(0.94-0.991)	0.023
$\delta Dt_{std}$ -PN	0.74 (0.55,1.18)	0.82 (0.63,3.45)	0.63 (0.52,0.89)	ale 88(1.031-1.332)	0.024
$\delta Dt_{sum}$ -PN	46.6 (29.1,80.7)	66.6 (42.0,110)	33.3 (25.7,48.6)	କ୍ଲାକ୍ସ୍ର କ୍ଲାକ୍ସ୍ୟୁକ୍ର (1.015-1.039)	< 0.001
δ Ag _{max} -C	1.70 (1.21,4.83)	1.79 (1.27,9.10)	1.52 (1.16,2.98)	a 2009(1-1.022)	0.089
δ Ag _{min} -C	-1.24 (-3.81,0.00)	-1.70 (-8.89,-1.01)	-0.91 (-1.75,0.00)	3(0.962-0.997)	0.051
δ Ag _{std} -C	0.54 (0.36,1.32)	0.80 (0.37,3.16)	0.45 (0.34,0.70)	<b>9</b> 1:1 <b>2</b> 7(1.026-1.252)	0.025
δ Ag _{sum} -C	15.6 (9.64,38.6)	29.8 (13.5,71.6)	11.9 (7.79,17.5)	A1.044(1.006-1.025)	0.003
δ Ps _{max} -C	33.0 (1.00,48.8)	33.0 (1.41,125)	31.0 (1.00,34.0)	and a section a	0.004
$\delta Ps_{std}$ -C	3.35 (0.24,6.16)	3.57 (0.29,11.7)	3.20 (0.24,4.86)	<b>ق</b> 1. <b>6</b> 3(1.019-1.14)	0.013
δ Ps _{sum} -C	39.1 (6.00,86.1)	74.4 (8.31,161)	33.4 (4.00,66.0)	<b>a</b> 1.∰ (1.005-1.015)	< 0.001
δ Ar _{max} -NP	136 (74.0,220)	182 (102,314)	105 (59.0,180)	<b>4</b> .00 (1.0002,1.003)	0.027
δ Ar _{std} -NP	29.6 (20.0,56.7)	31.7 (23.4,70.1)	25.7 (17. <mark>1,41.4)</mark>	► .0 <b>9</b> 4 (1.000,1.010)	0.067
δ Ar _{sum} -NP	2469 (1443,4286)	3369 (2230,5728)	1672 (1277,2987)	1.0 <b>g</b> 02 <b>(<u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u><u></u></u></b>	0.005
Ar _{max} -NP	3873 (3001,5765)	4269 (3260,6056)	3828 (2894,5406)	1.000 01 0.999989, 1.000213)	0.077
$\delta Ps_{sum}$ -NP	41.7 (22.2,79.9)	59.8 (39.8,104)	26.4 (20.1,51.1)	ເຊັ້າ.0 ເມີ່3(1.006-1.021)	0.001
δ Ar _{max} -N	435 (243,750)	539 (269,990)	404 (221,526)	<b>130</b> 01(1-1.002)	0.022
$\delta Ar_{min}$ -N	-170.00 (-369.00,-25.00)	-267.00 (-565.25,-108.75)	-79.00 (-224.00,-15.00)	0.9 <b>9</b> 8(0.996-0.999)	0.002
$\delta$ Ar _{std} -N	125 (80.2,225)	160 (90.5,273)	114 (74.6,158)	1.095(1.002-1.008)	0.003
$\delta Ar_{sum}-N$	12585 (7372,23204)	19058 (10208,29054)	9520 (6202,15009)	1.000084 <b>a</b> (1.000046, 1.000122)	< 0.001
Ar _{max} -N	53635 (43655,65410)	56546 (44597,77766)	51431 (38201,58878)	1.000014 <b>E</b> 1.000002, 1.000026)	0.025
$\delta$ ArRto _{max} -PN	0.01 (0.00,0.02)	0.01 (0.00,0.03)	0.00 (0.00,0.01)	4.494e+1 a a b i i (5.890e+2,3.427+29) i a b i i i i i i i i i i i i i	0.008
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Doromotors	ALL	FFR-Positive	FFR-Negative	yright, og Ddds Ratio	Dx
rarameters	N=141	N=68	N=73	Given the second	ΓV
δ ArRto _{min} -F	PN -0.02 (-0.05,-0.01)	-0.02 (-0.07,-0.01)	-0.02 (-0.04,-0.01)	<u>م</u> <رَقُرُونَ 001 (0,0.062)	0.
δ ArRto _{std} -P	N 0.01 (0.00,0.02)	0.01 (0.00,0.02)	0.01 (0.00,0.01)	3.177 <b>e</b> +1 <b>(q</b> 1.758e+3,5.740e+29)	0.
δ ArRto _{sum} -F	PN 0.63 (0.32,1.72)	0.85 (0.39,2.36)	0.58 (0.29,0.88)	<b>8</b> 5 <b>8</b> (1.175,2.117)	0.
δ Ar _{max} -PP	<b>P</b> 195 (126,404)	281 (141,704)	153 (111,286)	المعرفة المعرفة (1.001,1.003)	0.
δ Ar _{min} -PP	-171.00 (-295.00,-106.00)	-196.00 (-563.75,-109.50)	-153.00 (-226.00,-104.00)	କ୍ଷ୍ମିକ୍ରି <u>ହ</u> ୍ଛି (0.996,0.999)	0.
δ Ar _{std} -PP	54.3 (33.7,124)	77.3 (35.5,167)	43.7 (32.1,79.7)	តា 🖺 💇 (1.003,1.012)	0.
δ Ar _{sum} -PP	<b>4689 (2685,8783)</b>	6608 (3410,14024)	3487 (2556,5786)	1.009 经包.000053, 1.000187)	<0
Ar _{min} -PP	5151 (2774,7571)	4626 (2618,6928)	5754 (3719,8258)	0.999 🖉 🛐 d.999933, 1.000003)	0
δ Ps _{max} -PP	3.16 (2.24,5.00)	3.61 (3.00,100)	3.00 (2.24,3.61)	ລູ່ເຊັ່ງ ອີເຊັ່ງ ອີງອີງອີງ (1.005-1.019)	0.
δ Ps _{std} -PP	0.82 (0.60,1.15)	0.98 (0.66,8.50)	0.75 (0.57,0.90)	📲 🛱 🛱 7(1.05-1.221)	0.
δ Ps _{sum} -PP	40.4 (23.1,88.6)	73.8 (29.9,195)	32.8 (21.7,54.2)		<0
δ Ar _{max} -P	244 (90.0,430)	312 (150,692)	172 (70.0,362)	ي <mark>ق</mark> · 1 <mark>2</mark> 001(1-1.002)	0.
$\delta Ar_{std}$ -P	120 (80.2,203)	135 (82.3,267)	109 (75.7,159)		0
δ Ar _{sum} -P	11899 (6525,19157)	15787 (7938,28576) 🗸	9566 (5985,15629)	1.00(2)46 (1.000017, 1.000074)	0.
MAg _{max} -T7	-62.32 (-70.64,-34.61)	-48.00 (-66.89,15.5)	-67.39 (-72.03,-53.13)	<b>ب</b> و1.0 <mark>3</mark> 9(1.009-1.029)	<0
CAg _{max} -TT	45.0 (33.3,71.0)	58.2 (39.2,118)	43.1 (32.0,51.1)	al.078(1.009-1.028)	<0
MAg _{min} -TT	-70.76 (-76.85,-56.92)	-68.28 (-75.62,-41.24)	-71.98 (-77.61,-64.94)	ន្មា.0 <mark>ខ</mark> ្ម9(1.000-1.018)	0.
MAg-R _p	-61.41 (-71.15,-42.88)	-53.44 (-70.66,-38.24)	-65.92 (-71.78,-50.54)	at .0\$5(1.003-1.028)	0.
RtoAm-R _p T _p	N 6.49 (4.32,9.57)	7.35 (4.92,10.4)	5.68 (3.71,8.14)	₱1.055(1.005-1.126)	0.
RtoAm-R _p T _p	P 7.97 (5.88,12.0)	8.66 (6.03,12.9)	7.69 (5.56,11.1)	no 1.05 (1.004-1.133)	0.
RtoAm-R _p T	Sp 3.64 (2.38,4.70)	4.13 (3.08,5.01)	3.28 (2.36,4.50)	<b>e</b> .2 <b>2</b> 7(1.047-1.445)	0.
MAg-T _p	-64.66 (-71.34,-45.44)	-55.82 (-70.28,-12.79)	-67.91 (-72.69,-53.13)	³⁰ 1.045(1.006-1.026)	0.
CAg _{max} -T _p	43.1 (29.4,52.0)	45.0 (27.6,74.7)	42.2 (30.7,46.9)	1.029(1.001-1.017)	0.
RtoAm-T _p	0.76 (0.57,1.08)	0.81 (0.52,1.22)	0.75 (0.57,0.98)	1.5 \$9(0.978-2.618)	0.

 $\begin{aligned} & \text{The function } P_{p} = 0 \text{ for (clear, proc)} & \text{The function } P_{p} = 0 \text{ for (clear, proc)} \\ & \text{Dt} = \text{Distance, } P_{s} = \text{Position, } Ag = \text{Angle, } Am = \text{Magnitude, } Ar = \text{Area, } Rto = \text{Ratio, } P = \text{Positive, Positive Pole} = PP, \\ & \text{Pole, } M = \text{Magnetic Field, } C = \text{Current, max} = \text{Maximum, min} = \text{Minimum, sum} \\ & \text{Sum of all, std} = \text{Standard deviation} \\ & \text{Sum of all, std} = \text{Standard deviation} \\ & \text{Sum of all, std} = \text{Standard deviation} \\ & \text{Sum of all, std} = \text{Standard deviation} \\ & \text{Sum of all, std} = \text{Standard deviation} \\ & \text{Sum of all, std} = \text{Standard deviation} \\ & \text{Sum of all, std} = \text{Standard deviation} \\ & \text{Sum of all, std} = \text{Standard deviation} \\ & \text{Sum of all, std} = \text{Standard deviation} \\ & \text{Sum of all, std} = \text{Standard deviation} \\ & \text{Sum of all, std} = \text{Standard deviation} \\ & \text{Sum of the T max amplitude (T onset) to T max (T peak)}, \\ & \text{R}_{p} = \text{R} \text{ peak, } T_{p} = \text{T peak} \\ & \text{Sum of the T max amplitude (T onset) to T max (T peak)}, \\ & \text{R}_{p} = \text{R} \text{ peak, } T_{p} = \text{T peak} \\ & \text{Sum of the T max amplitude (T onset) + \text{Sum of the T max} (T peak)}, \\ & \text{Sum of the T max amplitude (T onset) + \text{Sum of the T max} (T peak)}, \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T max} (T peak), \\ & \text{Sum of the T$ 

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Supplementary Table 3 Diagnostic Model for	Assessment	of Myocardial Isch	hemia in Borderline Coron	ary Arter Lesions
Parameters	Diagnostic model			433 hclu
	В	OR	95%CI	I <del>s</del> va <b>B</b> e

	Demonsterne	Diagnostic model			433 clu
	Parameters	В	OR	95%CI	Is value
_	MAg _{max} -TT	1.385	3.995	(1.592-10.023)	<b>a</b> .009
	$\delta Dt_{sum}$ -PN	0.671	1.956	(1.270-3.012)	₩ E E E E E E E E E E E E E E E E E E E
	δAg _{sum} -C	0.411	1.508	(0.989 - 2.298)	
	δAr _{sum} -N	0.641	1.899	(1.251-2.883)	
	$\delta Ar_{min}$ -N	0.515	1.674	(1.121-2.500)	
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