



OPEN Peripheral microvessel area better predicts the severity of coronary stenosis of acute myocardial infarction patients over pulse wave velocity

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Microvascular obstruction (MVO) is linked with adverse clinical outcome in acute coronary syndrome (ACS) patients, therefore, early prediction of MVO with non-invasive peripheral microcirculation is crucial in facilitating optimal treatment. Current study aims to analyze the significance of opisthenar microvessel area (OMA, measured using optical coherence tomography, OCT) in predicting coronary stenosis (Gensini score, GS) and short-term cardiac recovery of ACS patients and the results were compared to those of arterial stiffness parameters (Pulse Wave Velocity, PWV; Ankle-Brachial Index; ABI). Results showed that cardiac functional parameters (e.g. ejection fraction, EF; fractional shortening, FS) and OMA were higher in normal/low risk (GS 0–≤ 20, n = 69) compared to medium/high risk patients (GS > 20, n = 44, $P < 0.0001$). Furthermore, OMA, EF or FS was *negatively* associated with the severity of coronary stenosis ($P < 0.0001$). In addition, OMA was negatively correlated with heart and liver damage parameters (e.g. creatine kinase, CK; creatine kinase muscle brain, CKmB; lactate dehydrogenase, LDH; hydroxybutyrate dehydrogenase, HDBH; aspartate aminotransferase, AST; alanine aminotransferase, ALT) or with inflammatory markers (neutrophil, neutrophil/lymphocyte ratio, NEU, NEU/LYM (NLR); systemic immune inflammation index, SII and system inflammation response index, SIRI), indicating clinical significance of OMA. Conversely, PWV and ABI were not associated with coronary stenosis or organ damage markers. Receiver Operator Characteristic (ROC) analysis showed high specificity and sensitivity of OMA for coronary stenosis (specificity 0.864 or sensitivity 0.87). In conclusion, OMA shows negative associations with the severity of coronary stenosis and adverse clinical parameters indicate that microcirculation measurement from opisthenar possesses prognostic value for severe ACS patients.

Keywords Coronary stenosis, Opisthenar microcirculation, Pulse wave velocity, Optical coherence tomography angiography, Cardiac function

Acute coronary syndrome (ACS) is one of the most severe types of heart diseases which leads to sudden cardiac death and heart failure worldwide. Recent prevalence of percutaneous coronary intervention (PCI) and pharmacological treatment restore coronary perfusion and the pumping function of the heart, but myocardial damage during coronary occlusion and post-reperfusion remains a major obstacle for optimal clinical outcome of ACS patients^{1,2}. Microvascular dysfunction is one of the severe comorbidities post-hemodynamic disorders in ACS patients and is the target for intensive research.

Investigations of microvascular pathophysiology using non-invasive or invasive image techniques (e.g. myocardial contrast echocardiography or pressure sensor/thermistors-tipped guidewire^{3,4}) indicated 30–40% incidence of microvascular obstruction (MVO) and delayed microvascular perfusion (dmVP), incidences peak

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within 24–72 h with or without sufficient recovery^{4,5}. Importantly, ACS patients with MVO and dMVP showed reduced EF and increased mortality rate during 6, 12 to 65 months' follow up^{6,7}, suggesting that insufficient microvascular perfusion post-PCI or antithrombotic therapy define adverse outcome including heart failure or recurrence of coronary occlusion. Early detection and preventive measure of microvascular dysregulation is crucial to guide the interventions for optimal treatment and the improvement of clinical outcome. However, direct assessment of microvascular circulation in the heart is technically demanding, noninvasive procedures become a necessity.

Peripheral microcirculation provides optimal alternative to analyze the pathological progression of ACS patients⁸. For example, recent reports presented optical coherence tomography (OCT) measurement of retinal fundus vascular density showed significant reduction in myocardial infarction (MI) patients compared to those of healthy controls⁹. In addition, peripheral arterial tonometry to measure flow-mediated dilatation in the finger tips has been shown to be associated with adverse clinical outcome in ACS patients^{10,11}. The downregulation of microcirculation was associated with increased risk of coronary artery disease (CVD). Capillary density from the dorsum of the middle phalanx was reduced in patients with premature CVD, and impaired peripheral microvascular blood flow predicts the incidence of cardiovascular events¹². Recently, our lab has investigated the opisthenar microcirculation area (OMA, i.e. the back of the hand microvessel area) which showed significant reduction in hypertensive patients¹³. Furthermore, OMA and heart rate normalized OMA (OMA-HR) were shown to be associated with cardiac functional parameters in ACS patients treated with PCI¹⁴. Until recently, the implications of OMA on the extent of coronary stenosis has not been studied, which may provide prognostic values for better management of ACS patients.

In this study, we grouped the patients according to the Gensini score since such an angiographic and comprehensive scoring system is well established to assess the extent of atherosclerotic plaque, the severity of stenosis and clinical outcome¹⁵. By analyzing OMA in low and high Gensini score patients, the correlations with the extent of coronary stenosis, organ damage and inflammatory markers, we aimed to provide direct information of peripheral microcirculation index in the significance of pathogenesis in ACS patients.

Methods

Study design and participants

Database of 160 in hospital ACS patients admitted to the Cardiology Department of Yanbian University Affiliated Hospital in China from October 2022 to October 2023 were recruited to the analysis. As shown in Fig. 1, both OMA and arterial stiffness parameters were measured in the Central Laboratory of the Science and Technology Building. 47 cases were excluded from the analysis according to the exclusion criteria: Severe cardiac dysfunction (patients EF < 30% in intensive care units); Malignant arrhythmia, Valvular heart disease, Severe metabolic diseases; History of kidney disease, eGFR < 30 mL/min; Patients with hematological, tumor and immune diseases; Severe liver function damage; Infectious disease patients; Severe peripheral vascular disease affecting peripheral circulation; Mental illness or neurological damage; Poor microcirculation measurement and incomplete clinical data. Therefore, 113 patients were included in the study. Base on electrocardiographic diagnosis and myocardial damage markers, ACS patients could be categorized to acute myocardial infarction (AMI) and unstable angina with ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI) patients. Those with no significant changes in electrocardiogram and myocardial injury markers were unstable angina. Among 113 patients, n = 32 are AMI, n = 21 are STEMI and n = 11 are NSTEMI. 67 were angina (unstable angina 47, stable angina 20) patients. 14 did not show angiography abnormalities.

Gensini score (GS) is the sum of the degree of coronary arterial disease \times corresponding coefficients of each branch. The degree of coronary arterial disease is defined as follow: 0 points for no vascular obstruction, 1 point for 1% to 24% vascular obstruction, 2 points for 25% to 50% vascular obstruction, 4 points for 51% to 75% vascular obstruction. Those with 76% to 90% blood vessel blockage were scored 8 points, those with 91% to 99% blood vessel blockage were scored 16 points, and those with complete blood vessel occlusion were scored 32 points. Corresponding coefficients was defined as follow: the common left main trunk coefficient is 5; the proximal, middle and distal coefficients of the left anterior descending branch are 2.5, 1.5 and 1.0, the first and second diagonal branches are 1.0 and 0.5 respectively; the proximal, middle and distal coefficients of the left circumflex branch are the same as the left anterior descending branch, the remaining posterior descending branch is 1.0, and the posterior collateral branch is 0.5; the right coronary coefficient is 1.0, and the collateral coefficients of other small blood vessels are all recorded as 0.5. As such, the subjects were divided into 4 groups according to the calculated GS (Table 1): normal (GS = 0), low-risk group ($1 \leq GS \leq 20$), medium risk group ($21 \leq GS \leq 39$), and high-risk group ($40 \leq GS \leq 99$). After calculating the scoring results, 113 patients were divided into 2 groups: normal + low risk group, GS ≤ 20 points, n = 69; medium + high risk group, GS > 20, n = 44.

Patients of normal + low risk group (0–20 points, n = 69) and medium + high risk group (> 21 points, n = 44) were compared with hemodynamic parameters including OMA, OMA-HR, cardiac functional parameters and arterial stiffness parameters (pulse wave velocity, PWV; ankle brachial index, ABI). Laboratory parameters including the blood cell counts, biochemical indexes for heart, liver and kidney functions and metabolic substrates (glucose, total glycerol, triglyceride, low-density lipoprotein, LDL and high-density lipoprotein, HDL) were measured from the venous blood on hospital admission and before the medical interventions. Color Doppler ultrasound examination was performed for the heart function analysis in the ultrasound medical department 2–3 days after the coronary arterial interventions.

This study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the Affiliated Hospital of Yanbian University, and the written informed consent and medical research questionnaire were signed before the test population is examined. The personal information of the test population is completely confidential.

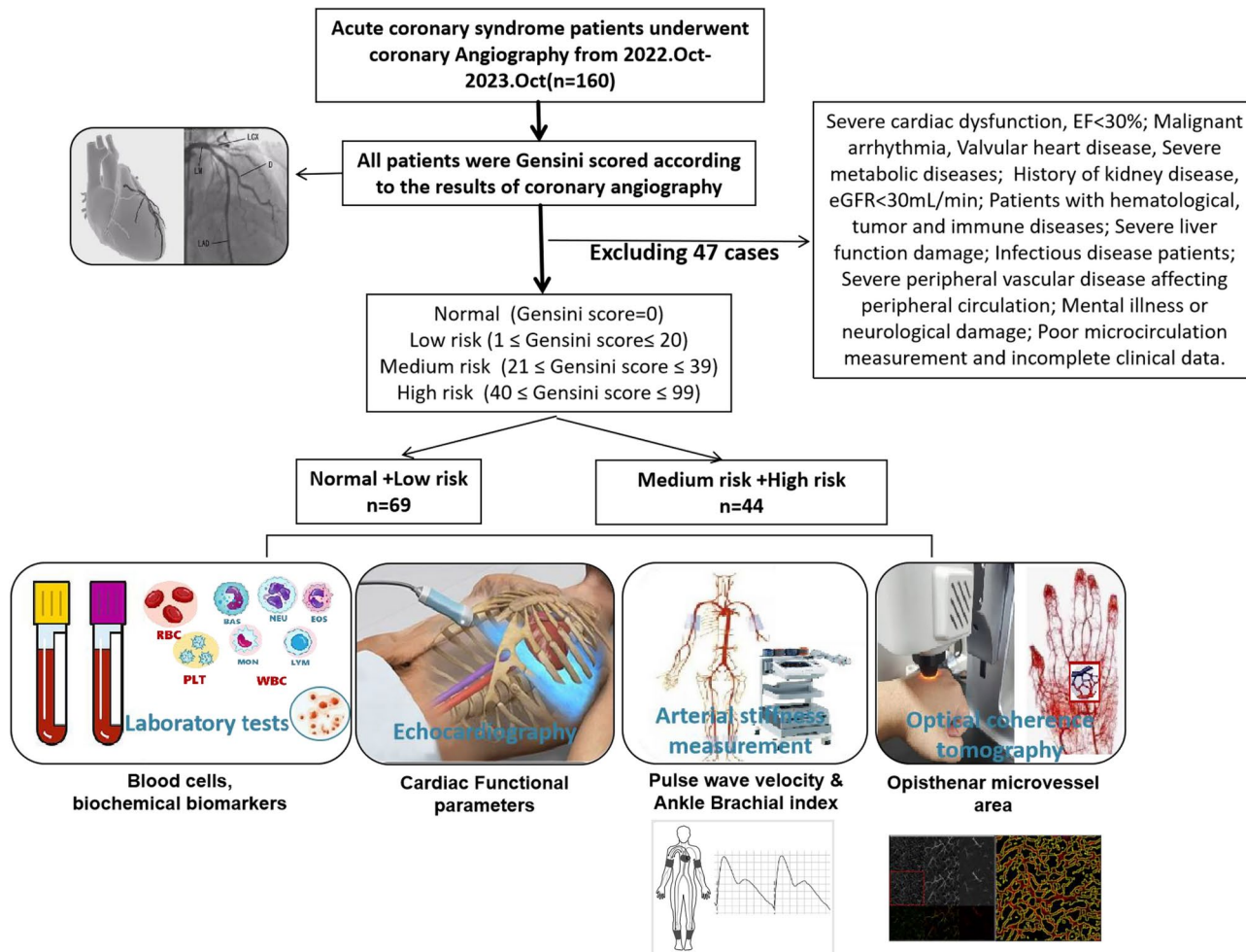


Fig. 1. Design of the study including ACS patients’ exclusion criteria and examination methods used in the study.

Lesion site	Coefficient	Stenosis degree	Score
Left trunk	5.0	0%	0
Proximal left anterior descending branch or circumflex branch	2.5	1–24%	1
Middle left anterior descending branch or circumflex branch	1.5	25–50%	2
Distal left anterior descending branch or circumflex branch	1.0	51–75%	4
Right coronary artery	1.0	76–90%	8
First diagonal branch or posterior descending branch	1.0	91–99%	16
Second diagonal branch or the posterior branch or blunt edge branch	0.5	100%	32

Table 1. Gensini score evaluation criteria. Gensini score is the sum of coronary stenosis degree score and lesion site score. The lesion score is the product of a single lesion score and coefficient: the coefficient indicates the importance of stenosis in different positions of the coronary artery system. Gensini score with ≤ 20 points was regarded as low risk; > 20 as medium to high risk.

Optical coherence tomography (OCT) angiography measurement of OMA area

All participants used a non-invasive imaging system (OCT model, Micro VCC, UK, Fig. 1) to obtain opisthenar microcirculation image from the back of their hands (1 cm from the middle bone, Fig. 1). The testing personnel adjust the relevant parameters of the instrument, adjust the lens of the device to closely fit the back of the patient’s hand as much as possible, and prevent the pressure applied by the lens from affecting the microcirculation blood flow at the back of the hand.

Briefly, a high-speed super luminescent diode (central wavelength: 1060 nm, repetition rate: 100 kHz, spectral bandwidth: 100 nm) scanned the field of view (4 mm × 4 mm) with 16 μm /pixel resolution. Laser

reflectance of the surface of flowing red blood cells depict microvessels under the skin. Longitudinal (x-axis) and cross-sectional area (y axis) were scanned and blood vessels in the upper layer of epidermal structure (small arteries, venules and capillaries generated blood vessel diagram) were processed for image acquisition. The total microvascular area measured in the field and the vessel density, total number of connections, total blood vessel length, average blood vessel length, total number of end points of the measurements were quantified and calculated automatically in the software (Angio Tool). Each patient measure opisthenar microcirculation twice at room temperature (23–25 °C) 2–3 days after coronary interventions.

Arterial stiffness measurement

Brachial ankle pulse wave velocity (baPWV) and ankle brachial index (ABI) were measured using an automated device (HBP-8000, Omron, Japan) on the same day when OMA was measured. The patient is in a supine position for 5–10 min in a quiet state. The cuff is placed at the site of brachial and ankle artery pulsation, ensuring that the device is in normal use and the machine is connected. By inputting gender, date of birth, height information and measuring, blood pressure, pulse wave velocity (PWV) and ankle brachial index (ABI) was obtained. Record the average value of two consecutive measurements.

Statistical analysis

SPSS 23.0 (IBM) statistical software was used for data analysis. Data were represented as mean \pm standard deviation (mean \pm SD) or in quartiles (P25, P75). Non-parametric statistical analysis and multivariate analysis were used for comparison between groups. Pearson correlation analysis was used to analyze the association of each test parameter, The Receiver operating characteristic (ROC) curve was used to explore the relationship between OMA, OMA-HR, and coronary arterial stenosis. $P < 0.05$ was considered statistically significant.

Results

General information and clinical characteristics of two study groups

Table 2 showed that among general information, HR, DBP, MAP, and SaO₂ were statistically significant between normal + low risk and medium + high risk groups ($p < 0.05$). Biochemical examination results showed significant differences in biomarkers of heart, liver and kidney functions (in particular, CK, CK-MB, LDH, HBDH, ALT, AST and Crea, $p < 0.05$). In blood routine tests, WBC, NEU and LYM, as well as RD-CV were significantly different between groups ($p < 0.05$).

Comparison of parameters of cardiac function, arterial stiffness and microvessels

Table 3 showed that EF, FS, and CO levels were lower and LVDS, EDV, ESV, E and E/e' were greater in medium + high risk group ($p < 0.05$). PWV or ABI were not different between two groups ($p > 0.05$). Notably, OMA and OMA-HR were significantly reduced in medium + high risk group ($p < 0.001$).

Correlation with the severity of coronary stenosis

Correlation analysis in Table 4 showed that severity of coronary stenosis was negatively correlated with: (1) EF ($r = -0.45, p < 0.01$), FS ($r = -0.41, p < 0.01$), SV ($r = -0.068, p < 0.05$), and CO. ($r = -0.325, p < 0.01$); (2) OMA ($r = -0.373, p < 0.01$) and OMA-HR ($r = -0.221, p < 0.05$). PWV or ABI were not correlated with the severity of coronary stenosis ($p > 0.05$).

Since inflammation is known to be correlated strongly with the disease progression, we compared the markers from blood routine results. As shown in Table 4, except for LYM, which showed a significant negative correlation, the severity of coronary stenosis was positively correlated with NEU, NLR, MLR and SIRI ($p < 0.05$).

Correlation between cardiac function, arterial stiffness and microvessels with biochemical indicators

Correlation analysis were conducted between biochemical parameters and cardiac function, arterial stiffness and microvessels in all patients. As shown in Table 5, OMA and OMA-HR showed significant and negative correlations with heart and liver function parameters (CK, CK-MB, LDH, HDBH, AST, ALT, $p < 0.05$); similar correlations were observed with heart functional parameters such as EF and FS with heart, kidney and liver functional indexes (CK-MB, CREA, AST, TP, $p < 0.05$). However, PWV or ABI showed no correlation with any of organ function parameters.

Correlation analysis between inflammation and cardiac function, arterial stiffness and microvessels parameters

Table 6 showed results of inflammatory indicators and cardiac function in all patients. EF or FS showed negative correlations with NEU, NEU/LYM ratio (NLR), MON/LYM ratio (MLR) and SIRI ($p < 0.05$). Similar analysis between inflammatory indicators and OMA or OMA-HR were conducted (Table 6) and the results showed that OMA or OMA-HR were negatively correlated with NEU, NLR, SII and SIRI ($p < 0.05$).

Intriguingly, PWV was shown to be negatively correlated with MON ($p < 0.05$) whereas ABI was negatively correlated with NEU, NLR and SII ($p < 0.05$).

AUC analysis of OMA and OMA-HR

We went on and analyzed the sensitivity and specificity of OMA and OMA-HR for the degree of coronary stenosis (Fig. 2). AUC of OMA is 0.717 (specificity 0.864, sensitivity 0.551), with a cutoff value of 27,693 pixels. AUC of OMA-HR is 0.681 (sensitivity 0.87, specificity 0.5), with a cutoff value of 339.64 pixels/m.

	Variable	Normal + Low risk n = 69	Medium risk + High risk n = 44	P
General information	AGE(y)	59.43 ± 7.65	59.88 ± 8.09	0.894
	HTN history	37	19	0.281
	Smoking history	30	23	0.363
	Sex	M = 40 F = 29	M = 32 F = 12	0.113
	BMI (kg/m ²)	25.75 ± 2.94	24.80 ± 3.87	0.133
	HR (60–100)/min	71.26 ± 9.25	74.86 ± 11.53	0.046*
	SBP (90–120) mmHg	135 (117.5, 152.5)	125.5 (114, 137)	0.097
	DBP (60–90) mmHg	78 (72.5, 89)	75 (70, 79.7)	0.014*
	MAP (70–105) mmHg	98.51 ± 14.47	92.26 ± 10.99	0.031*
Heart	CK (0–200) U/L	77 (55, 118.5)	149.5 (75.5, 1363.5)	0.000**
	CK-MB (0–25) U/L	14 (9, 18)	20.5 (11.5, 113.7)	0.001**
	LDH (0–220) U/L	179 (157, 220)	245.5 (183.5, 578.5)	0.000**
	HBDH (0–295) U/L	145 (128.5, 175)	236 (142.5, 492.5)	0.000**
Kidney	BUN (2.5–7.0) mmol/L	5.2 (4.3, 5.95)	5.3 (4.5, 6.5)	0.360
	CREA (75–115) mmol/L	65 (53.5, 72)	68 (60, 79.5)	0.026*
Liver	AST (0–40) U/L	19 (16, 24.5)	45.5 (22, 181.7)	0.000**
	ALT (0–40) U/L	18 (14, 27)	39.5 (21, 55.75)	0.000**
	TB (5.1–25.6) umol/L	11.1 (8.35, 14.7)	11.45 (7.77, 14.17)	0.793
	TP (60–80 g)/L	64 (61, 70.5)	63 (60, 68.5)	0.178
Metabolism	GLU (3.9–6.1) mmol/L	5.11 (4.68, 5.58)	5.28 (4.68, 6.13)	0.197
	TG (0.48–1.88) mmol/L	1.44 (1.05, 1.97)	1.38 (0.88, 1.72)	0.406
	TC < 5.18 mmol/L	3.83 (3.12, 5.06)	4.21 (3.21, 5.39)	0.300
	LDL (0.00–3.12) mmol/L	2.18 (1.83, 2.78)	2.53 (1.85, 3.45)	0.084
	HDL > 0.9 mmol/L	1.05 (0.9, 1.24)	1.03 (0.96, 1.21)	0.588
	SaO ₂ (95–100%)	0.97 (0.95, 0.98)	0.975 (0.97, 0.98)	0.004**
Blood routine	WBC (4–10) × 10 ⁹ /L	6.37 (5.43, 8.08)	7.28 (6.0, 9.67)	0.039*
	RBC (3.5–5.5) × 10 ¹² /L	4.51 ± 0.57	4.41 ± 0.51	0.189
	HGB (110–160) g/L	141.84 ± 17.75	139.31 ± 15.93	0.511
	PLT (100–300) × 10 ⁹ /L	207 (181, 242)	199.5 (183.5, 232)	0.768
	RDW-SV (37–50fL)	43 (40.5, 44.5)	44 (41, 45)	0.056
	RDW-CV (11.5–14.5%)	13 (12, 13)	13 (12.25, 14)	0.033*
	NEU (1.8–6.3) × 10 ⁹ /L	4.04 (2.92, 5.44)	5.2 (3.58, 7.69)	0.005**
	LYM (1.1–3.2) × 10 ⁹ /L	1.71 (1.45, 2.47)	1.54 (1.1, 2.0)	0.024*
	MON (0.1–0.6) × 10 ⁹ /L	0.46 ± 0.18	0.49 ± 0.20	0.235
	EOS (0.02–0.5) × 10 ⁹ /L	0.1 (0.05, 0.18)	0.075 (0.02, 0.15)	0.240
	BAS (0–0.06) × 10 ⁹ /L	0.03 (0.02, 0.04)	0.025 (0.02, 0.04)	0.181

Table 2. Comparison of general information, biochemical indicators, blood routine between two group patients. Normal + Low risk: Gensini score ≤ 20, Medium + High risk: Gensini points > 20; P . Normal + Low risk vs. Medium + High risk **P* < 0.05, ***P* < 0.01.

Discussion

The main findings of this study are the identification of OMA (measured using optical coherence tomography OCT from ACS patients 2–3 days after the medical interventions), which was significantly reduced in medium + high risk coronary stenosis patients, that is associated with the GS determination of the severity of coronary stenosis. The results showed that EF, FS, SV, CO as well as OMA were negatively correlated with the severity of coronary stenosis and NEU, NEU/LYM ratio, MON/LYM ratio and SIRI were positively correlated with the severity of coronary stenosis. OMA was also associated with heart and liver damage parameters in ACS patients. Arterial stiffness indexes, PWV or ABI were not affected and were not associated with the severity of coronary stenosis. AUC analysis indicated high sensitivity and specificity of OMA and OMA-HR with the coronary stenosis in ACS patients. Taken together, through comprehensive analysis of cardiac function, main arterial properties, peripheral microvessels, inflammatory indexes and biochemical organ damage indexes, we provide robust evidence to suggest that non-invasive OMA can be a valuable parameter to predict the severity of coronary arterial diseases.

Hemodynamic coherence following acute coronary syndrome is important and sufficient blood flow through microcirculation is essential in maintaining target organ functions. In general, cardiac function is assessed using echocardiography where EF and FS are regarded as golden standard to represent the functional recovery following the therapy of ACS patients. In fact, measured indexes are often within normal range in the groups examined, but EF, FS, CO and SV were significantly higher in normal + low risk group compared to those of

	Variable	Normal + Low risk n = 69	Medium risk + High risk n = 44	P
Echocardiography	EF (0.57–0.75)	0.62 (0.60, 0.63)	0.59 (0.57, 0.61)	0.000**
	FS (0.20–0.40)	0.31 (0.30, 0.32)	0.30 (0.27, 0.31)	0.000**
	SV (70–90) ml	73 (70, 74)	70 (68, 74)	0.087
	CO (3–6) l/min	5.2 (4.9, 5.3)	5.0 (4.5, 5.1)	0.000**
	DT (180–240) ms	210 (188, 239)	200 (188, 227)	0.268
	LVDD	46 (43, 48.5)	47 (45, 49.7)	0.107
	LVDS	28 (26, 30)	30 (28, 32)	0.007**
	EDV	117.74 (113.33, 120.97)	121.67 (114.87, 129.69)	0.005**
	ESV	45.33 (43.18, 48)	49.66 (45.5, 55)	0.000**
	E	0.6 (0.5, 0.7)	0.7 (0.6, 0.8)	0.013**
	A	0.8 (0.7, 0.9)	0.8 (0.7, 0.9)	0.212
	e'	0.10 (0.09, 0.13)	0.10 (0.08, 0.12)	0.074
	E/A	0.83 (0.67, 0.97)	0.89 (0.75, 1.14)	0.171
	E/e'	5.69 (5.0, 7.5)	7.5 (6.0, 9.17)	0.000**
Arterial stiffness	BaPWV R (M/S)	1563 (1387, 1819)	1601 (1419, 1877)	0.398
	BaPWV L (M/S)	1578 (1394, 1758)	1593 (1480, 1838)	0.244
	ABL.R	1.11 ± 0.10	1.09 ± 0.09	0.477
	ABL.L	1.09 ± 0.09	1.08 ± 0.09	0.540
Microvessels	OMA (pixel)	27,549.05 ± 2301.48	25,995.11 ± 1745.01	0.000**
	OMA-HR (pixel/m)	392.31 ± 57.18	355.81 ± 62.45	0.001**

Table 3. Comparison of cardiac function, arterial stiffness and OMA in two groups patients. * $P < 0.05$, ** $P < 0.01$.

	Variable	Degree of coronary stenosis	
		r	p
Echocardiography	EF (0.57–0.75)	−0.450	0.000**
	FS (0.20–0.40)	−0.410	0.000**
	SV (70–90) ml	−0.068	0.006**
	CO (3–6) l/min	−0.325	0.001**
	DT (180–240) ms	−0.130	0.180
Arterial stiffness	BaPWV R (M/S)	0.134	0.158
	BaPWV L (M/S)	0.156	0.098
	ABL.R	−0.062	0.514
	ABL.L	−0.010	0.919
Microvessel	OMA (pixel)	−0.373	0.000**
	OMA-HR (pixel/m)	−0.221	0.019*
Inflammation	NEU	0.210	0.026*
	LYM	−0.202	0.032*
	MONO	0.147	0.121
	NLR	0.220	0.019*
	MLR	0.288	0.002**
	PLR	0.120	0.204
	SII	0.140	0.138
SIRI	0.302	0.001**	

Table 4. Correlation with the severity of coronary stenosis. * $P < 0.05$, ** $P < 0.01$.

medium + high risk group (Table 3), which was accompanied by lower end-diastolic and end-systolic volume or length indexes (e.g. EDV, ESV, LVDD). These results are consistent with greater heart, kidney and liver damage indexes in medium + high risk patients. Furthermore, NEU is greater and LYM is smaller, indicative of inflammatory profiling changes with the extent of the diseases. Importantly, OMA and OMA-HR were significantly reduced in medium + high risk patient group where cardiac function was reduced, suggesting impaired microcirculation in peripheral organs due to insufficient hemodynamic coherence. The analysis results suggest that OMA or OMA-HR could be additional functional indicators of the recovery of ACS patients. This

Variable N = 113	CK		CK-MB		LDH		HDBH		BUN		CREA		AST		ALT		TB		TP	
	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
EF (0.57-0.75)	-0.183	0.053	0.146	0.122	-0.094	0.323	0.113	0.235	0.065	0.494	-0.209	0.026*	-0.220	0.019*	-0.089	0.349	-0.125	0.189	-0.231	0.014*
FS (0.20-0.40)	-0.101	0.288	0.231	0.014*	-0.049	0.607	0.117	0.217	0.099	0.297	-0.178	0.060	-0.255	0.006**	-0.092	0.333	-0.077	0.418	-0.207	0.027*
BaPWV R (M/S)	-0.028	0.776	0.012	0.903	-0.032	0.739	-0.073	0.442	0.146	0.123	0.007	0.942	-0.010	0.920	-0.041	0.688	0.006	0.952	0.050	0.596
BaPWV L (M/S)	-0.087	0.358	-0.057	0.549	-0.085	0.370	-0.105	0.268	0.170	0.072	0.130	0.168	-0.040	0.671	-0.069	0.470	-0.058	0.543	0.092	0.333
ABI.R	-0.157	0.096	-0.174	0.066	-0.108	0.255	-0.044	0.642	0.027	0.780	0.058	0.544	-0.160	0.090	-0.164	0.083	-0.048	0.615	-0.019	0.844
ABI.L	-0.159	0.093	-0.154	0.102	-0.097	0.306	-0.096	0.313	0.026	0.788	-0.015	0.873	-0.166	0.078	-0.071	0.458	-0.215	0.022*	-0.058	0.545
OMA (pixel)	-0.121	0.202	-0.075	0.431	-0.204	0.030*	-0.176	0.062	-0.103	0.277	-0.027	0.780	-0.223	0.018*	-0.089	0.348	-0.177	0.060	0.152	0.109
OMA-HR(pixel/m)	-0.225	0.017*	-0.234	0.012*	-0.198	0.035*	-0.227	0.016*	-0.122	0.198	-0.084	0.375	-0.262	0.005**	-0.218	0.020*	-0.094	0.320	0.051	0.592

Table 5. Correlation analysis between biochemical indicators with cardiac function, arterial stiffness and OMA in all patients. * $P < 0.05$, ** $P < 0.01$.

Variable N = 113	NEU		LYM		MONO		NLR		MLR		SII		SIRI	
	r	P	r	P	r	P	r	P	r	P	r	P	r	P
EF (0.57–0.75)	-0.183	0.053*	0.146	0.122	-0.094	0.323	-0.209	0.026*	-0.220	0.019*	-0.125	0.189	-0.231	0.014*
FS (0.20–0.40)	-0.101	0.288	0.231	0.014*	-0.049	0.607	-0.178	0.060	-0.255	0.006**	-0.077	0.418	-0.207	0.027*
BaPWV R (M/S)	-0.042	0.660	-0.134	0.158	-0.217	0.021*	0.053	0.587	-0.163	0.084	0.054	0.568	-0.175	0.064
BaPWV L (M/S)	0.035	0.715	-0.113	0.234	-0.187	0.047*	0.093	0.325	-0.154	0.105	0.058	0.541	-0.109	0.248
ABI.R	-0.259	0.006**	0.021	0.825	-0.047	0.619	-0.189	0.045*	0.016	0.863	-0.167	0.077	-0.164	0.083
ABI.L	-0.276	0.003**	0.010	0.916	0.018	0.853	-0.226	0.016*	0.058	0.542	-0.188	0.047*	-0.161	0.088
OMA (pixel)	-0.151	0.110	0.136	0.152	0.014	0.885	-0.182	0.053	-0.136	0.151	-0.119	0.210	-0.198	0.035*
OMA-HR (pixel/m)	-0.276	0.003**	0.125	0.186	-0.005	0.958	-0.225	0.017*	-0.145	0.126	-0.210	0.026*	-0.277	0.003**

Table 6. Correlation analysis between inflammation and cardiac function, arterial stiffness and OMA in all patients. * $P < 0.05$, ** $P < 0.01$.

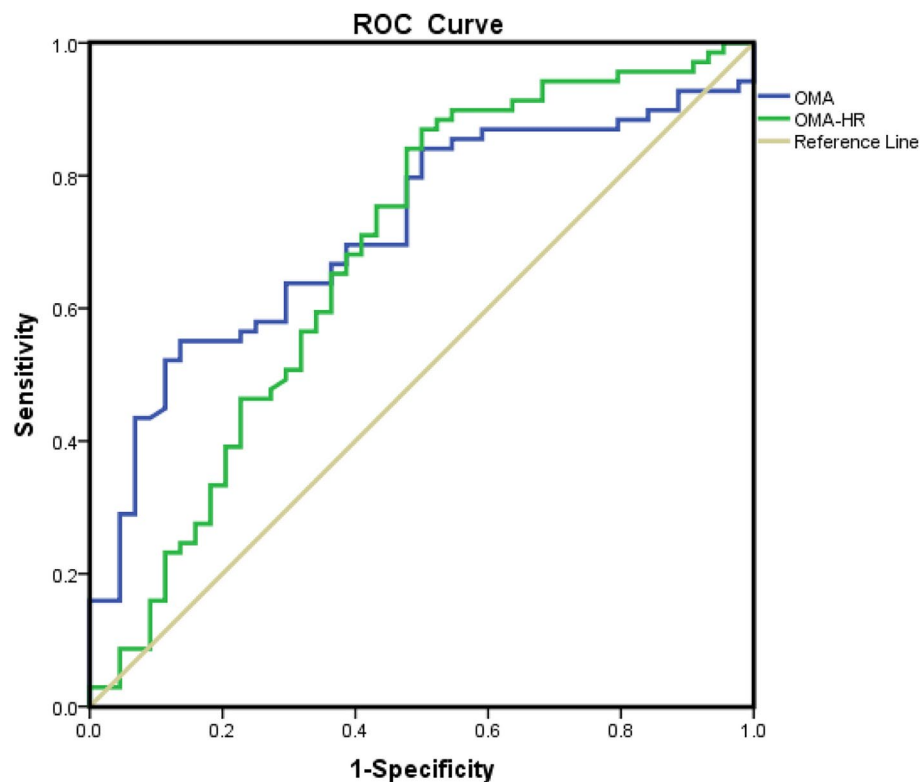


Fig. 2. Receiver Operator Characteristic (ROC) curve predicting coronary stenosis. Opisthenar microvessel area (OMA): area under the curve (AUC) 0.717, cut-off 27,693 pixel, sensitivity 0.551, specificity 0.864. Heart rate normalized OMA (OMA-HR): area under the curve 0.681, cut-off 339.64 pixel/m, sensitivity 0.87, specificity 0.5.

is important because peripheral microcirculation such as retinal microvessels measured from coronary heart disease patients or systemic hypertensive patients showed similar reduction^{16–18}. It should be noted that neither PWV nor ABI were shown to be different between normal + low risk and medium + high risk patient groups. As such, arterial stiffness indexes which represent arterial properties of the patients are not affected by the disease or the recovery of the disease, per se.

Changes in the microcirculation post-therapy in ACS patients are important in understanding the functional recovery and cardiovascular stratification. Accumulating evidences showed that in majority of STEMI patients post-PCI, microvascular perfusion of the heart was reduced when detected with cardiac magnetic resonance (CMR) imaging¹⁹. Endothelial dysfunction or microvascular thrombi may cause the disruption of coronary reperfusion and clinical consequence can be huge due to the progression of irreversible myocardial hemorrhage at the infarct core, which could be associated with mortality and re-hospitalization due to heart failure²⁰.

Due to the impracticality of measuring microcirculation of the heart post-therapy, peripheral sources such as skin microcirculation can be optimal alternative. Indeed, skin microcirculation is considered to be a representative vascular bed for assessing microvascular reactivity and has been proposed as a prognostic marker of the restoration of normal microcirculation in ACS patients^{21,22}. In the current study, the significance of OMA is further confirmed by showing clear associations between OMA/OMA-HR and the severity of coronary stenosis (Table 4). Similar associations were observed with EF, FS, SV and CO as well as inflammatory indexes such as NEU, LYM, NLR, MLR and SIRI (Table 6), supporting predictive values in ACS patients. It should be noted that OMA or OMA-HR were significantly associated with heart, liver functional parameters from blood test results and inflammatory indexes on admission to the hospital, further indicating the prognostic values in assessing the severity of ACS patients. PWV or ABI were not associated with the severity of coronary stenosis, discriminating macro- and microvessels in such a clinical significance.

Over the last two decades, techniques and consensus of measuring microcirculation in various diseases are overwhelmed, with non-invasive and robust optimal coherence tomography angiography (OCTA) being central to detect morphological and functional changes of the organ microcirculation (such as retina, sublingual, cerebrum, gut, and opisthenar). As the current analysis suggests, microcirculation results are convincing in assessing clinical implications or outcomes in patients including acute coronary syndrome^{7,8}. E.g. impaired retinal or cerebral microcirculation is shown to be prevalent in high risk coronary arterial disease population²³. The AUC analysis further supports the high specificity and sensitivity of OMA and OMA-HR on assessing the disease status.

Taken together, Gensini score classification of ACS patients revealed that peripheral microcirculation, OMA, associates with the severity of coronary stenosis. Larger population studies are needed to determine hemodynamic

coherence for comprehensive understanding of the functional recovery of ACS patients. Microcirculation is important in better therapeutic management in severe ACS patients.

Data availability

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Received: 17 June 2024; Accepted: 6 November 2024

Published online: 19 November 2024

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Author contributions

C.C., J.W., T.T.H., B.L.Z., Z.Y.G., X.J., Z.H.Z., are involved in the patients' database analysis, measurement, data analysis and writing. M.H.L., J.X.L. are involved in statistics, L.C., W.H.X., X.N.H., Y.H.Z. are involved in project design, manuscript review and finalization.

Funding

National Natural Science Foundation of China, Grant/Award Number: NSFC31860288 and NSFC32260213; National Natural Science Foundation of China, Grant/Award Number: 82100307; Korean National Research Foundation of Korea (NRF), Grant/Award Number: 2023R1A2C2007021; Korean Society of Hypertension (Grant number KSH-R-2020); BK21 Four for Seoul National University College of Medicine.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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