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Original Article

Parameters of myocardial contrast echocardiography associated with coronary microcirculatory dysfunction following revascularization in patients with acute ST-segment elevation myocardial infarction

Haiyun Meng[1], Yanbo Wang[2], Lifang Su[3], Xinshun Gu[4]

ABSTRACT

Objective: To identify factors associated with coronary microcirculatory dysfunction(CMD), as evaluated by myocardial contrast echocardiography(MCE), in patients with ST-segment elevation myocardial infarction(STEMI) after emergency revascularization.

Methodology: A total of 144 consecutive patients with STEMI who underwent percutaneous coronary intervention (PCI) at the Department of Cardiology, the Second Hospital of Hebei Medical University between January 2022 to December 2024 were retrospectively enrolled, comprising 70 in the CMD group(62 men, 88.6%) and 74 in the normal group (65 men, 87.8%) based on MCE findings, MCE was performed within 24 hours after PCI. Clinical characteristics, MCE, and coronary angiography were collected and compared between groups. Multivariable logistic regression analysis(backward stepwise) was applied to determine independent predictors of post-PCI CMD.

Results: Anterior wall myocardial infarction (AWMI) was found in 59 (84.3%) patients in the CMD group and 37 (50%) in the normal group ($P< 0.001$). Total protein levels were modestly but significantly increased in patients with CMD. TTE assessment showed a lower ratio of early to late diastolic transmitral flow velocities in the CMD group. The myocardial perfusion score index was markedly elevated in the CMD group. Regarding infarct-related arteries, the left anterior descending artery was more frequently involved in the CMD group, whereas involvement of the right coronary artery was less common. Multivariable logistic regression identified NE ≥8.61 $\times 10^9$/L and AWMI as independent risk factors of post-PCI CMD in patients with STEMI.

Conclusion: NE ≥8.61 $\times 10^9$/L and AWMI appear to independently predict the development of CMD in patients with STEMI.

KEYWORDS: Acute ST-segment elevation myocardial infarction, Coronary microcirculatory dysfunction, Emergency percutaneous coronary intervention, Myocardial contrast echocardiography.

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INTRODUCTION

Acute ST-segment elevation myocardial infarction(STEMI) remains a major cause of morbidity and mortality worldwide. In recent years, the establishment of regional STEMI care networks, together with improvements in prehospital emergency transport systems and reperfusion strategies, has enabled earlier recanalization of the infarct-related arteries (IRAs). Advances in reperfusion approaches, including primary percutaneous coronary intervention (PCI), rescue PCI, routine PCI following thrombolysis, and adjunctive antithrombotic therapy, have substantially increased the likelihood of achieving rapid, complete, and sustained coronary reperfusion.[1]

Despite timely, adequate restoration of epicardial blood flow, existing literature indicates that the coronary microcirculation often sustains varying degrees of

injury. This impairment may lead to microvascular hypoperfusion, which, in turn, contributes to a decline in left ventricular ejection fraction (LVEF) and increases the risk of heart failure (HF) and even death.[2] Therefore, early identification of microcirculatory alterations after revascularization is of considerable clinical significance in the management of STEMI. Presently, coronary microcirculatory function is commonly assessed by measuring coronary flow reserve and microvascular resistance via transthoracic echocardiography (TTE), coronary computed tomography, and intracoronary pressure-wire approaches. However, these methods are limited by suboptimal specificity.

In contrast, myocardial contrast echocardiography (MCE), a noninvasive, bedside-applicable technique, offers distinct clinical advantages. By employing intravenously administered microbubble contrast agents, MCE enhances myocardial and ventricular imaging, allowing more precise visualization of myocardial perfusion and facilitating early detection of cardiac pathology.[3] Against this background, MCE parameters associated with coronary microcirculatory dysfunction (CMD) following emergency PCI were investigated in patients with STEMI.

METHODOLOGY

This was a retrospective study. Patients with STEMI who underwent emergency PCI at the Department of Cardiology, the Second Hospital of Hebei Medical University, between January 2022 and December 2024 were consecutively enrolled in this study.

Ethical approval: The study was approved by the Institutional Ethics Committee of Baoding No.1 Central Hospital (No.[2024]190; Date: August 02, 2024). The studies were conducted in accordance with the local legislation and institutional requirements.

Inclusion criteria:

- Age ≥18 years.
- Diagnosis of STEMI based on the *Fourth Universal Definition of Myocardial Infarction*;
- Undergoing primary PCI within 12 hours of symptom onset, or PCI performed 2–24 hours after thrombolytic therapy;
- Completion of MCE within 24 hours after PCI. According to the *Fourth Universal Definition of Myocardial Infarction*, myocardial infarction is defined by acute myocardial injury, detected by elevated cardiac troponin above the 99th percentile upper reference limit, with a rise and/or fall in values, accompanied by clinical evidence of acute myocardial ischemia, including at least one of the following:
- (a) symptoms of acute myocardial ischemia;
- (b) new ischemic electrocardiographic changes;
- (c) development of pathological Q waves;
- (d) imaging evidence of new loss of viable myocardium or new regional wall motion abnormalities;
- (e) identification of coronary thrombus by coronary angiography (CAG), intracoronary imaging, or autopsy.[4]

Exclusion criteria:

- Presence of cardiogenic shock.
- Coexisting severe organ dysfunction or malignant disease.
- Contraindications to MCE.
- Incomplete clinical data records.

Data were retrieved from the hospital information and management system. Necessary data were obtained for both groups, including baseline clinical characteristics, laboratory findings, and data from TTE, MCE, and CAG. (1) Baseline clinical data included sex, age, body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP) at admission, cardiac function classification based on the Killip grading system, medical history [*e.g.,* hypertension, coronary artery disease (CAD), diabetes mellitus (DM), and cerebral infarction (CI)], and lifestyle factors (*e.g.,* smoking, and alcohol consumption). Medications administered during hospitalization were also recorded, including aspirin, indobufen, clopidogrel, ticagrelor, statins, β-blockers, angiotensin receptor-neprilysin inhibitors (ARNI), angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), recombinant human brain natriuretic peptide (rhBNP), furosemide, spironolactone, and sodium-glucose cotransporter-2 inhibitors (SGLT-2i). (2) Laboratory parameters comprised white blood cell count (WBC), peak creatine kinase-MB (CK-MB), high-sensitivity C-reactive protein (hs-CRP), N-terminal pro-B-type natriuretic peptide (NT-proBNP), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), D-dimer (D-D) levels, and adenosine diphosphate-induced platelet aggregation (ADP-PA). (3) Standard TTE provided measurements of left atrial diameter (LAD), left ventricular end-diastolic diameter (LVEDD), right atrial diameter (RAD), right ventricular longitudinal diameter (RVD), the ratio of early (E) to late (A) diastolic transmitral flow velocities (E/A), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), stroke volume (SV), and left ventricular ejection fraction (LVEF). (4) MCE mainly involved the semi-quantitative metric, the myocardial perfusion score index (MPSI). (5) CAG data included total ischemic time and IRAs, including the left main coronary artery (LM), left anterior descending artery (LAD), left circumflex artery (LCX), or right coronary artery (RCA).

MCE was performed using a very low mechanical index imaging mode. In accordance with the 2019 *Expert Consensus on Clinical Application of Cardiac Ultrasound Contrast Agents*[5], 2-mL of reconstituted contrast agent (SonoVue suspension) was administered via slow intravenous injection at a rate of 1-mL/min, followed by a 5-mL flush of 0.9% sodium chloride solution. Dynamic images were sequentially acquired

in the apical two-chamber, three-chamber, and four-chamber views. Each view included 20 consecutive cardiac cycles, comprising two to three cycles before the "flash" impulse and 15 cycles after the flash. All MCE examinations and subsequent image analyses were performed by a single senior echocardiographer with extensive experience, ensuring consistency in data acquisition and interpretation.

A semi-quantitative method was used to assess myocardial perfusion. The left ventricle was divided into 17 segments, and each segment was assigned a perfusion score (PS): PS = 1 indicated normal perfusion, PS = 2 indicated heterogeneous perfusion, and PS = 3 indicated perfusion defect or absence of perfusion. The MPSI was calculated by summing the PS values across all segments and dividing by the total number of segments (n= 17). An

Table-I: Comparison of baseline characteristics between the two groups.

	CMD Group (n = 70)	*Normal Group (n = 74)*	*t/Z/χ²*	*P-value*
Age (years, $\bar{x}\pm s$)	57.6±11.2	59.6±12.1	−1.016	0.311
Male [n(%)]	62(88.6%)	65(87.8%)	0.019	0.892
BMI (kg/m², $\bar{x}\pm s$)	26.3±3.5	26.1±3.7	0.380	0.704
SBP at admission (mmHg, $\bar{x}\pm s$)	127.7±16.7	127.2±18.3	0.156	0.876
DBP at admission (mmHg, $\bar{x}\pm s$)	85.0±14.4	81.5±14.0	1.453	0.148
Infarct location			19.029	<0.001
Anterior wall [n(%)]	59(84.3%)	37(50.0%)		
Inferior wall [n(%)]	11(15.7%)	37(50.0%)		
Killip class [n(%)]			−0.281	0.778
I	52(74.3%)	57(77.0%)		
II	17(24.3%)	14(18.9%)		
III	1(1.4%)	3(4.1%)		
Hypertension [n(%)]	38(54.3%)	36(48.6%)	0.458	0.499
CAD [n(%)]	10(14.3%)	8(10.8%)	0.397	0.529
DM [n(%)]	20(28.6%)	18(24.3%)	0.334	0.563
CI [n(%)]	11(15.7%)	9(12.2%)	0.380	0.538
Smoking [n(%)]	33(47.1%)	26(35.1%)	2.145	0.143
Alcohol consumption [n(%)]	15(21.4%)	17(23.0%)	0.050	0.824
Aspirin [n(%)]	62(88.6%)	71(95.9%)	2.773	0.096
Indobufen [n(%)]	8(11.4%)	3(4.1%)	2.773	0.096
Clopidogrel [n(%)]	7(10.0%)	7(9.5%)	0.012	0.913
Ticagrelor [n(%)]	63(90.0%)	67(90.5%)	0.012	0.913
Statins [n(%)]	68(97.1%)	74(100%)	2.144	0.143
β-blockers [n(%)]	64(91.4%)	61(83.6%)	2.010	0.156
ARNI/ACEI/ARB [n(%)]	61(87.1%)	54(73.0%)	4.491	0.034
rhBNP [n(%)]	45(64.3%)	29(39.2%)	9.070	0.003
Furosemide [n(%)]	29(41.4%)	32(43.2%)	0.049	0.826
Spironolactone [n(%)]	36(51.4%)	34(45.9%)	0.433	0.511
SGLT-2i	34(48.6%)	35(47.3%)	0.023	0.878

overall MPSI > 1.0 was defined as indicative of CMD.[6] Based on MCE findings, patients were categorized into the CMD group or the normal group.

Statistical analysis: All statistical analyses were conducted using SPSS 25.0. Continuous data with a normal distribution were expressed as mean ± standard deviation ($\bar{x}\pm s$) and compared between groups using the independent-samples *t*-test. Non-normally distributed continuous data were presented as median with interquartile range [M (Q1,Q3)] and analyzed using the Mann-Whitney U test. Categorical data were expressed as percentages (%) and compared using the chi-square (χ^2) test or Fisher's exact test. Multivariate logistic regression analysis with a backward stepwise approach was performed to identify independent factors associated with CMD in patients undergoing emergency PCI for STEMI. A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 144 patients were included, comprising 70 patients in the CMD group (62 men, 88.6%) and 74

Table-II: Comparison of laboratory findings between the two groups.

	CMD Group (n = 70)	*Normal Group (n = 74)*	*t/Z/χ^2*	*P-value*
CK [U/L, M(Q1,Q3)]	3183.5(1755.0,5134.8)	2107.0(1179.5,3249.5)	−2.630	0.009
CK-MB [U/L, M(Q1,Q3)]	458.8(283.0,601.0)	226.5(115.0,327.8)	−1.939	0.053
NT-proBNP [pg/mL, M(Q1,Q3)]	419.0(160.0,1378.5)	278.0(93.5,901.3)	−1.885	0.059
Fib [g/L, M(Q1,Q3)]	3.0(2.5,3.3)	2.8(2.4,3.4)	−0.252	0.801
FDP [mg/L, M(Q1,Q3)]	1.6(0.9,3.6)	1.9(1.0,4.7)	−1.435	0.151
D-D [g/mL, M(Q1,Q3)]m	0.22(0.09,0.48)	0.21(0.10,0.53)	−0.568	0.570
WBC [10^9/L, M(Q1,Q3)]	11.7(8.8,14.2)	9.9(8.1,11.9)	−2.353	0.019
NE [10^9/L, M(Q1,Q3)]	9.8(7.4,12.0)	8.1(6.1,9.9)	−2.862	0.004
LY [10^9/L, M(Q1,Q3)]	1.3(0.9,1.8)	1.3(1.0,1.8)	−0.174	0.862
hs-CRP [mg/L, M(Q1,Q3)]	2.6(1.87.8)	3.8(2.0,9.4)	−0.981	0.327
Hb [g/L, M(Q1,Q3)]	142.5(134.0,150.0)	138.5(127.5,146.3)	−1.841	0.066
HCT (%, $\bar{x}\pm s$)	42.1±4.4	41.0±4.1	1.566	0.120
Plt (10^9/L, $\bar{x}\pm s$)	223.6±62.4	219.1±56.2	0.450	0.653
Scr [mol/L, M(Q1,Q3)]m	75.5(66.8,89.3)	75.0(67.0,89.0)	−0.202	0.840
SUA [mol/L, M(Q1,Q3)]m	311.0(269.0,387.3)	318.0(268.5,397.5)	−0.136	0.892
TP [g/L, M(Q1,Q3)]	66.5(63.8,70.1)	64.7(60.8,67.3)	−2.768	0.006
ALB [g/L, M(Q1,Q3)]	41.0(38.3,42.2)	39.8(36.8,41.5)	−1.787	0.074
G [g/L, M(Q1,Q3)]	26.0(23.7,28.1)	25.9(22.8,28.6)	−1.061	0.289
ALT [U/L, M(Q1,Q3)]	48.5(26.0,68.3)	41.0(26.0,64.6)	−1.211	0.226
AST [U/L, M(Q1,Q3)]	118.0(59.4,334.0)	153.2(65.5,221.3)	−0.252	0.801
TC [mmol/L, M(Q1,Q3)]	4.7(3.8,5.4)	4.6(3.9,5.3)	−0.256	0.798
TG [mmol/L, M(Q1,Q3)]	1.2(1.0,1.8)	1.5(0.7,2.0)	−0.126	0.900
HDL-C [mmol/L, M(Q1,Q3)]	1.1(0.9,1.3)	1.0(0.9,1.3)	−0.698	0.485
LDL-C [mmol/L, M(Q1,Q3)]	2.9(2.4,3.6)	2.9(2.3,3.4)	−0.686	0.493
Lp(a) [mg/dL, M(Q1,Q3)]	22.8(10.0,37.4)	14.0(8.6,27.6)	−2.406	0.016
FPG [mmol/L, M(Q1,Q3)]	6.9(5.6,9.4)	6.3(5.4,8.2)	−1.057	0.290
ADP-PA [%, M(Q1,Q3)]	52.8(32.3,71.2)	43.0(18.9,69.9)	−1.275	0.202

Table-III: Comparison of TTE and MCE findings between the two groups.

	CMD Group (n = 70)	*Normal Group (n = 74)*	*t/Z/χ²*	*P-value*
LAD [mm, M(Q1,Q3)]	34.0(31.0,38.0)	35.0(33.0,38.0)	−1.189	0.234
LVEDD [mm, M(Q1,Q3)]	50.0(46.8,52.0)	48.5(46.0,52.0)	−0.896	0.370
RAD [mm, M(Q1,Q3)]	33.0(29.8,35.0)	33.0(31.0,35.3)	−0.608	0.543
RVD [mm, M(Q1,Q3)]	20.0(19.0,22.0)	20.0(19.0,22.0)	−0.352	0.725
LVEF [%, M(Q1,Q3)]	48.3(41.4,57.6)	52.6(43.8,61.8)	−1.605	0.109
E/A [M(Q1,Q3)]	0.7(0.6,1.1)	0.8(0.6,1.3)	−2.244	0.025
LVEDV [mL, M(Q1,Q3)]	127.7(121.5,133.8)	126.2(117.2,133.1)	−1.073	0.283
LVESV [mL, M(Q1,Q3)]	69.9(64.0,73.6)	67.3(62.6,72.0)	−1.935	0.053
SV [mL, M(Q1,Q3)]	59.0(54.4,62.0)	57.1(52.3,60.7)	−1.085	0.278
MPSI [M(Q1,Q3)]	1.47(1.32,1.77)	1.00	−2.244	<0.001

patients in the normal group (65 men, 87.8%). The two groups showed no statistically significant differences in age, sex composition, BMI, SBP and DBP at admission, Killip classification, prior medical history (including hypertension, CAD, DM, and CI), or smoking and alcohol consumption (all $P > 0.05$). However, anterior wall myocardial infarction (AWMI) was significantly more prevalent in the CMD group than in the normal group [59(84.3%) *vs.* 37(50.0%), $P < 0.001$]. In addition, the proportion of patients receiving ARNI, ACEI, or ARB, as well as rhBNP, was significantly higher in the CMD group [61(87.1%) *vs.* 54 (73.0%), $P = 0.034$; 45 (64.3%) *vs.* 29 (39.2%), $P = 0.003$). No significant differences were observed between the groups with respect to other in-hospital medications (all $P > 0.05$) (Table-I).

Compared with the normal group, patients in the CMD group exhibited significantly higher levels of creatine kinase (CK), WBC, neutrophil count (NE), and total protein (TP) [3183.5(1755.0, 5134.8) *vs.* 2107.0(1179.5, 3249.5), $P = 0.009$; 11.7 (8.8, 14.2) *vs.* 9.9 (8.1, 11.9), $P = 0.019$; 9.8 (7.4, 12.0) *vs.* 8.1 (6.1, 9.9), $P = 0.004$; 66.5 (63.8, 70.1) *vs.* 64.7 (60.8, 67.3), $P = 0.006$]. No statistically significant differences were observed between the two groups for the remaining laboratory parameters (all $P > 0.05$) (Table-II).

Compared with the normal group, patients in the CMD group demonstrated a significantly lower E/A ratio [0.7(0.6, 1.1) *vs.* 0.8 (0.6, 1.3), $P < 0.025$]. In contrast, the MPSI was markedly elevated in the CMD group [1.47(1.32, 1.77) *vs.* 1.00, $P < 0.001$]. No significant differences were identified between the two groups for other TTE parameters (all $P > 0.05$) (Table-III).

The proportion of patients with the IRA involving the LAD was significantly higher in the CMD group than in the normal group [55 (78.6%) *vs.* 30 (40.5%), $P < 0.001$]. In contrast, involvement of the RCA was less frequent in the CMD group [15 (21.4%) *vs.* 40 (54.1%), $P < 0.001$]. No significant differences were observed between the two groups in terms of total ischemic time,

Table-IV: Comparison of CAG findings between the two groups.

	CMD Group (n = 70)	*Normal Group (n = 74)*	*t/Z/χ²*	*P-value*
Total ischemic time [min, M(Q1,Q3)]	420.0(322.5,600.0)	390.0(270.0,637.5)	−0.738	0.460
IRA	33.0(29.8,35.0)	33.0(31.0,35.3)	−0.608	0.543
LM [n(%)]	1(1.4%)	2(2.7%)	−	1.000
LAD [n(%)]	55(78.6%)	30(40.5%)	21.513	<0.001
LCX [n(%)]	8(11.4%)	12(16.2%)	0.689	0.406
RCA [n(%)]	15(21.4%)	40(54.1%)	16.220	<0.001
Implanted stents [n, M(Q1,Q3)]	1.0	1.0	−0.112	0.911
Total stent length [mm, M(Q1,Q3)]	26.0(18.0,36.0)	24.0(17.3,35.3)	−0.257	0.797
Contrast agent volume [mL, M(Q1,Q3)]	120.0(100.0,160.0)	120.0(100.0,160.0)	<0.071	0.943

the proportion of LM or LCX involvement, number of implanted stents, total stent length, or contrast agent volume (all $P > 0.05$) (Table-IV).

Variables with $P < 0.10$ in univariate analyses, including clinical characteristics, laboratory findings, TTE and MCE parameters, and CAG data, were entered into a multivariate logistic regression model using a backward stepwise (Wald) method. Continuous variables (number of stents, stent length, WBC, NE, CK, TP, and E/A ratio) were dichotomized based on clinically relevant thresholds (Table-V). Categorical variables included ARNI/ACEI/ARB use, rhBNP use, LM, LAD, LCX, and RCA involvement, as well as infarct location. The analysis demonstrated that NE ≥8.61 $\times 10^9$/L [odds ratio (OR) = 3.207, 95% confidence interval (95%CI): 1.541–6.672, $P = 0.002$] and AWMI (OR= 5.466, 95% CI: 2.408–12.410, $P < 0.001$) were independently associated with the development of CMD in patients with STEMI after PCI (Table-V).

Table-V: Variable assignment for multivariate logistic regression analysis.

Variable	*Coding*
Number of stents	0 = no stent; 1 = ≥1 stent
Stent length	0 = ≤24.0 mm; 1 = >24.0 mm
WBC	0 = ≤10.35 $\times 10^9$/L; 1 = >10.35 $\times 10^9$/L
NE	0 = ≤8.61 $\times 10^9$/L; 1 = >8.61 $\times 10^9$/L
CK	0 = ≤2512.5 U/L; 1 = >2512.5 U/L
TP	0 = ≤65.65 g/L; 1 = >65.65 g/L
E/A	0 = ≤2.0; 1 = >2.0
ARNI/ACEI/ARB use	0 = no; 1 = yes
rhBNP use	0 = no; 1 = yes
LM involvement	0 = no; 1 = yes
LAD involvement	0 = no; 1 = yes
LCX involvement	0 = no; 1 = yes
RCA involvement	0 = no; 1 = yes
Infarct location	0 = inferior wall; 1 = anterior wall

DISCUSSION

In our study involving 73 patients with anterior STEMI, 54 developed CMD. After a median follow-up of 3.6 months, a significantly higher proportion of patients in the CMD group had an LVEF <50%, suggesting that CMD adversely affects long-term ventricular function.[7] Consistent with these observations, our multivariate logistic regression analysis identified anterior wall infarction as a significant risk factor for post-PCI CMD in patients with STEMI. This aligns with earlier findings,[8,9] including those reported by Marrazzo G et al.[8], who employed MCE to assess CMD-related outcomes in patients undergoing PCI for STEMI. The study demonstrated that AWMI was more prevalent among patients with CMD. In our cohort, the proportion of IRAs involving the LAD was markedly higher in the CMD group, which is consistent with previous reports.[10] The coronary microcirculation is not merely a passive conduit for myocardial perfusion but a dynamic regulatory system governed by intricate metabolic and myogenic mechanisms. The higher incidence of the no-reflow phenomenon in anterior STEMI may, at least in part, be attributable to the relatively underdeveloped collateral circulation in the myocardial territory supplied by the LAD.[11] Taken together, heightened clinical vigilance and early intervention strategies are warranted to identify and prevent CMD, particularly in patients with AWMI.

Our study further demonstrated that both WBC and NE were significantly elevated in the CMD group compared with the normal group, with NE emerging as an independent risk factor for CMD in the multivariate logistic regression model. These findings are in line with previous reports.[12] For instance, a study employing

Table-VI: Multivariable logistic regression analysis of independent risk factors for CMD.

	β	*SE*	*Wald* χ^2	*P-value*	*OR*	*95%CI*
NE						
≥8.61 $\times 10^9$/L	1.165	0.374	9.717	0.002	3.207	1.541–6.672
<8.61 $\times 10^9$/L						
Infarct location						
Anterior wall	1.699	0.418	16.489	<0.001	5.466	2.408–12.410
Inferior wall						

positron emission tomography in combination with coronary flow reserve measurements showed that inflammatory activation can adversely affect coronary microvascular function even in asymptomatic individuals. Elevated WBC counts have been reported to correlate with infarct size in patients with STEMI. One plausible explanation is that activated WBCs induce oxidative and proteolytic myocardial injury by releasing reactive oxygen species, proteolytic enzymes, interleukins, and peroxidases. Alternatively, elevated levels of WBC, as an early inflammatory response to myocardial injury, become more pronounced as larger infarcts occur.[13] In this study, neutrophils appeared to play a particularly important role in the development of CMD after reperfusion. This observation is supported by prior work, including a study by Merdler I et al., which demonstrated that an elevated neutrophil-to-lymphocyte ratio is strongly associated with more severe CMD in patients undergoing PCI for STEMI.[14] Mechanistically, activated NEs and monocytes can alter red blood cell (RBC) rheology, increasing RBC aggregation and promoting tissue factor expression, thereby enhancing thrombus formation. To summarize, in addition to prompt reperfusion therapy, modulation of the inflammatory response is equally important in the early intervention of STEMI. Emerging evidence indicates that early initiation of proprotein convertase subtilisin/kexin Type-9 inhibitors on top of statin therapy can attenuate inflammatory activity and improve microvascular function following PCI in patients with acute coronary syndrome.[15]

This study also found that the proportions of patients receiving ARNI/ACEI/ARB and rhBNP were significantly higher in the CMD group than in the normal group. This observation may reflect more compromised cardiac function during the acute phase in patients with CMD. Although no significant difference in LVEF was observed between the two groups, it is plausible that a subset of patients in the CMD group had concomitant HF with preserved ejection fraction (HFpEF). Previous studies have suggested a close association between HFpEF and CMD, with underlying mechanisms involving altered vascular responsiveness to external stimuli, reduced capillary density, and inflammation.[16] Evidence also indicates that patients with CMD complicated by HFpEF tend to have worse outcomes compared with those with CMD alone.[17]

In addition, a study focusing on patients with acute coronary syndrome who developed CMD after PCI demonstrated that treatment with sacubitril/valsartan plus nicorandil significantly improved cardiac function, endothelial function, and inflammatory profiles.[18] A retrospective analysis also reported that approximately 60% of patients continue to exhibit CMD despite successful reperfusion following STEMI, and the presence of CMD was associated with a markedly increased risk of in-hospital acute HF.[19] These findings suggest that, in patients undergoing primary PCI for STEMI, early postoperative assessment with MCE may facilitate prompt identification of CMD, enabling earlier initiation of HF-targeted therapies and potentially improving outcomes in those with concomitant HFpEF.

In this study, MCE proved to be a cost-effective, safe, and bedside-accessible imaging modality capable of rapidly detecting abnormalities in myocardial perfusion, without being constrained by examination setting. These features make it particularly valuable for early diagnosis and prognostic evaluation in patients with STEMI. MCE integrates conventional echocardiography with intravenously administered microbubble contrast agents, allowing real-time, noninvasive assessment of myocardial microvascular perfusion and function. In the context of AMI, MCE offers several advantages, including dynamic evaluation of perfusion, sensitive detection of microvascular impairment, guidance for reperfusion strategies, identification of viable myocardium, and prognostic evaluation. Studies have shown that MCE parameters of myocardial viability are significantly associated with major adverse cardiovascular events in patients with AMI, underscoring its value in predicting long-term outcomes.[20] Following early PCI in patients with STEMI, restoration of epicardial coronary patency does not invariably translate into adequate microvascular reperfusion, and a subset of patients continues to exhibit the "no-reflow" phenomenon.[11] This condition is largely attributable to structural and functional disruption of the myocardial microvasculature. MCE, by utilizing microbubble contrast agents, enables direct assessment of microvascular integrity. A comparative study evaluating ultrasound-mediated microbubble therapy combined with recombinant human pro-urokinase versus pro-urokinase alone demonstrated that the combined approach significantly improved cardiac function in patients with LAD no-reflow after STEMI and reduced the incidence of adverse cardiovascular events during short-, mid-, and long-term follow-up.[21]

Limitations: First, this single-center observational study has a relatively modest sample size, which may limit the generalizability of the findings. Second, the analysis focused primarily on factors associated with CMD during hospitalization, and long-term prognostic data were not assessed, warranting extended follow-up in future studies. Third, although risk factors for CMD after revascularization using MCE were investigated by enrolling patients with STEMI who received primary PCI, assessment of coronary microvascular function using the index of microcirculatory resistance was not performed due to practical constraints.

CONCLUSIONS

Using MCE to quantify myocardial perfusion, the present study enabled the early identification of CMD in patients with STEMI following PCI. The findings indicate that NE ≥8.61 $\times 10^9$/L and AWMI may be independent risk factors for post-revascularization CMD.

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HM: Study design, Literature search and manuscript writing.
YW and **LS:** Data collection, data analysis and interpretation. Critical Review.
XG: Manuscript revision and validation and is responsible for the integrity of the study.
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