Original Research

Predictive Value of the No-Reflow Phenomenon and Epicardial Adipose Tissue for Clinical Outcomes After Primary Percutaneous Coronary Intervention

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Introduction: The determinants of clinical outcomes in patients with acute ST-elevation myocardial infarction (STEMI) are still being debated. The aim of this study was to investigate the prognostic value of the no-reflow phenomenon and epicardial adipose tissue (EAT) thickness for clinical outcomes in patients undergoing primary percutaneous coronary intervention (pPCI) for STEMI.

Methods: The present study prospectively included 114 consecutive patients (mean age 54 ± 10 years, 15 women) who underwent successful pPCI. Patients were divided into two groups according to the occurrence of the no-reflow phenomenon and further subdivided according to the tertile of EAT thickness (Group I <5.1 mm, Group II ≥5.1 mm). We assessed the composite and separate occurrence of major adverse cardiac events.

Results: Throughout the 3-year follow up, the number of admissions for heart failure was significantly higher in patients with no-reflow (n=5 [20%] vs. n=1 [1%], p=0.003) and in female patients (n=4 [26%] vs. n=2 [2%], p=0.004). In the subgroup analysis, group I patients with no-reflow showed a higher frequency of admission for heart failure (n=4 [44%] vs. n=1 [6%], p=0.04). However, multivariate logistic regression analysis demonstrated that only no-reflow and female sex independently predicted admission for heart failure (OR: 19.3, 95%CI: 1.4-269.7, p=0.03, and OR: 24.9, 95%CI: 2.2-288.8, p=0.01, respectively).

Conclusion: No-reflow and female sex are independent predictors of admission for heart failure in the long-term follow up of patients with STEMI. However, EAT thickness is not associated with clinical outcomes after pPCI.

Despite the enormous progress in the diagnosis and management of coronary atherosclerosis, the poor prognosis after ST-elevation myocardial infarction (STEMI) still remains a significant health concern worldwide. Although several factors have been identified as associated with worse clinical outcomes, many still remain undetermined.

It has been shown that myocardial reperfusion is one of the major determinants of positive clinical outcomes.[1-3] In patients with STEMI, inadequate myocardial reperfusion, a condition referred to as the "no-reflow" phenomenon, may overshadow the beneficial effect of the successful restoration of epicardial coronary flow.[4] Reduced ST-segment resolution is accepted as an ECG sign of the no-reflow phenomenon. ST-segment resolution re-

flects myocardial flow rather than epicardial flow.[5]

Recently, epicardial adipose tissue (EAT) has been suggested as an emerging cardiometabolic risk factor, while increased EAT was also shown to be strongly associated with coronary artery disease.[6-10] We previously reported that increased EAT thickness is associated with inadequate ST-segment resolution after primary percutaneous coronary intervention (pPCI).[11] EAT is a true visceral fat depot that is localised beneath the visceral pericardium. It has anatomical and functional contiguity with myocardium and coronary arteries and it is also a metabolically active endocrine and paracrine organ that secretes many anti- and pro-inflammatory as well as anti- and pro-atherogenic cytokines and hormones, resulting in vascular, immunological, and inflammatory responses.[12,13]

The role of EAT in the prognosis of atherosclerotic cardiovascular diseases has been less well studied[14] and, to the best of our knowledge, the relationship between no-reflow together with EAT and clinical outcomes in patients with STEMI after pPCI has not yet been explored. The aim of this study was to investigate the predictive value of the no-reflow phenomenon and EAT thickness for clinical outcomes after pPCI.

Methods

Study population

All patients consecutively admitted to the coronary care unit with a diagnosis of first acute STEMI who underwent pPCI were considered eligible and enrolled if they fulfilled the following criteria: (1) symptoms lasting for ≥30 min, consistent with acute STEMI within 12 hours of symptom onset; (2) new ST elevation ≥0.2 mV at the J point in at least two contiguous leads; (3) greater than threefold increase in serum creatine kinase (CK) levels; (4) angiographic evidence of total occlusion, i.e. TIMI grades 0 or 1; (5) successful angioplasty (stable TIMI III flow and <30% residual stenosis at the occlusion site); (6) no additional >50% stenosis in the infarct-related coronary artery distal to the culprit lesion. Six patients were excluded because of left ventricular hypertrophy criteria on the baseline ECG, defined as Sokolow–Lyon voltages >35 mV (n=3), or a missing (n=1) or uninterpretable ECG because of the development of left bundle-branch block (n=1) or a permanent pacemaker (n=1). The final study population therefore consisted of 114 patients. The study protocol was approved by the local ethics committee and informed consent was obtained from each patient.

Study protocol

A 12-lead ECG was recorded in each patient just after hospital admission. All patients received aspirin (300 mg) and clopidogrel (300 mg) prior to their transfer to the catheterisation laboratory. Emergency coronary angiography was performed using the percutaneous femoral approach. The infarct-related coronary artery was graded according to the TIMI classification[15] and collateral vessels were graded according to the classification of Rentrop.[16] Good collateral flow was defined as Rentrop collateral flow 2-3. Heparin (100 U/kg) was administered in all patients after the coronary anatomy was defined. Occlusion of the infarct-related coronary artery was crossed using a 0.014" guide wire and balloon angioplasty was performed if necessary. Routine stenting was attempted directly or following balloon angioplasty. An intravascular bare-metal stent was implanted at the site of the ruptured atherosclerotic plaque. Primary coronary angioplasty was defined as successful if restored blood flow was TIMI 3 in the infarct-related artery and residual stenosis following stent deployment was <30%. Additional stents were implanted as required. A repeat 12-lead ECG was obtained 60 minutes after successful pPCI. All of the patients were treated according to the recommendations of the latest ACC/AHA Guidelines for the Management of Patients with STEMI.[17] The use of glycoprotein IIb/IIIa receptor blockers was left to the discretion of the operator.

Electrocardiographic analysis

Electrocardiograms were analysed in a blinded manual manner by two experienced cardiologists. ST-segment elevation in mm was measured 20 ms after the J point. The sum of ST-segment elevations was calculated for leads I, aVL, and V_1-V_6 for anterior infarctions, and for leads II, III, aVF, V_5, and V_6 for inferior infarctions. The sum of ST-segment elevations in mm was obtained before pPCI (ΣSTR_b) and 60 minutes after the restoration of TIMI 3 flow (ΣSTR_a). A percentage ST-segment resolution ($STR = 100 \times \Sigma[STR_b - STR_a] / \Sigma STR_b$) <50% was accepted as an ECG sign of the no-reflow phenomenon. The percentage of persistent ST-segment elevation was defined as 100 - STR. Patients were separated into two groups according to the classification of Schröder et

al:[18] those with STR≥50% were defined as the normal reflow group and those with STR<50% as the no-reflow group.

Echocardiographic analysis

Transthoracic echocardiography was performed within 72 hours of admission, using an ESAOTE 2.5 MHz probe (ESAOTE, Genova, Italy) with the patient in the left lateral decubitus position. All examinations were performed by an experienced cardiologist who was blind to the patient's clinical information. All measurements were reassessed by an experienced second cardiologist, also blind to the patient's clinical information. The left ventricular ejection fraction was determined using the modified Simpson's method.[19] EAT thickness was measured according to the method previously described.[20] EAT, identified as an echo-free space on the right ventricular free wall beneath the visceral pericardium on 2-dimensional echocardiography, was measured from the parasternal long- and short-axis views at the end of systole. EAT thickness was measured from the parasternal long-axis view at a point on the free wall of the right ventricle along the midline of the ultrasound beam, perpendicular to the aortic annulus as the anatomical reference point (Figure 1). From the mid-ventricular parasternal short-axis view, it was measured at a point on the free wall of the right ventricle along the midline of the ultrasound beam, perpendicular to the interventricular septum at mid-chordal level, with the tip of the papillary muscle as the anatomic reference point. The maximum values at each site were measured and the average value was used for the statistical analysis. In the analysis of outcomes, patients were also grouped according to the tertile of EAT thickness (Group I <5.1 mm, Group II ≥ 5.1 mm).

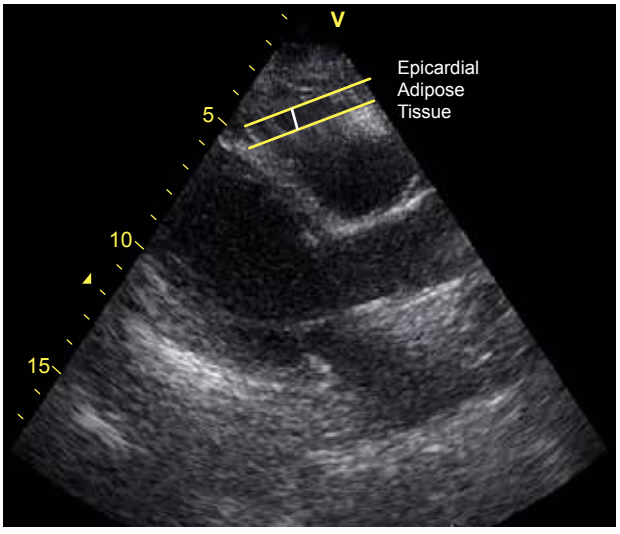

Figure 1. Transthoracic echocardiogram in parasternal long-axis view at end-systole, showing an echo-free area on the free wall of the right ventricle representing the epicardial adipose tissue (EAT).

Analysis of patient data

A clinical history of risk factors, including age, sex, diabetes mellitus, hypertension, hyperlipidaemia and smoking, was recorded for each patient. Cardiac symptoms lasting <30 minutes were defined as a sign of angina pectoris, and angina occurring within 48 hours before the onset of infarction was defined as pre-infarction angina. After treatment for acute STEMI, angina-onset-to-balloon time and door-to-balloon time were also recorded. Venous blood samples were obtained during the first 24 h for routine biochemical analyses. On the second day, waist circumference and height measurements were completed for body mass index calculations and for metabolic syndrome determination. Metabolic syndrome was diagnosed in patients with at least three of the following five criteria, defined according to the Adult Treatment Panel III report: (1) hypertension (history of hypertension, systolic blood pressure ≥130 mmHg, diastolic blood pressure ≥85 mmHg or on anti-hypertensive medication); (2) triglycerides ≥150 mg/dL; (3) high-density lipoprotein cholesterol (HDL-C) <40 mg/dL for men and <50 mg/dL for women; (4) fasting blood glucose ≥110 mg/dL; and (5) abdominal obesity (waist circumference >102 cm in men and >88 cm in women).[21] Waist circumference was measured at the midpoint between the bottom of the rib cage and the top of the iliac crest at breath hold after full expiration.

Follow up and outcomes

Data from the 3-year follow-up period were obtained from medical records or by interviewing patients, their family members, or their primary physicians. The clinical endpoints were the composite and separate occurrence of major adverse cardiac events, defined as cardiac death, non-fatal myocardial infarction, target vessel revascularisation, or admission for heart failure. Cardiac death was defined as mortality from acute myocardial infarction, heart failure, or sudden death, which was an unexpected death from

a cardiac cause in the absence of progressive circulatory failure lasting for 60 minutes or more. Non-fatal myocardial infarction was defined with reference to the presence of an increase in the serum creatine kinase-MB enzyme concentration to more than twice the upper limit of normal, in combination with either typical chest pain or discomfort lasting >30 min, or typical ischaemic electrocardiographic changes. Target vessel revascularisation was defined as repeat intervention (surgical or percutaneous) within a vessel treated during the index procedure that was driven by symptoms or objective signs of ischaemia. Admission for heart failure was defined as admission with clinical symptoms and signs, and chest radiographic findings of heart failure. All events were evaluated by two cardiologists blinded to all the patient's clinical information.

Statistical analysis

Quantitative variables were expressed as mean ± standard deviation and qualitative variables were expressed as percentage (%). Data were tested for normal distribution using the Kolmogorov–Smirnov test. Comparisons of parametric values between two groups were made using a two-tailed Student t-test, while for nonparametric values the Mann–Whitney U test was used. Categorical variables were compared using the chi-squared test or Fisher's test. Spearman rho and Pearson tests were used for correlation analysis. Binary logistic regression analysis was used to evaluate independent associations between admission for heart failure and clinical parameters. The relationship between the percentage of persistent ST-segment elevation and admission for heart failure was analysed using the area under the receiver operator characteristic curve. A p-value <0.05 was considered statistically significant. All statistical analyses were carried out using SPSS version 18.0 (SPSS, Chicago, IL, USA).

Results

The study population consisted of 114 patients (mean age 54 ± 10 years, range 35-83, 15 women) with STEMI who underwent pPCI. Patients were divided into 2 groups according to ST-segment resolution: those with no-reflow (n=25 [22%] and those without (n=89 [78%]).The baseline characteristics of the patients included in the study are presented in Table 1.

Body mass index (28.9 ± 2.7 vs. 27.1 ± 3.8 kg/m^2, p=0.03) and waist circumference (101.4 ± 10.2 cm vs. 96.6 ± 9.1 cm, p=0.03) were found to be significantly higher in the no-reflow group. As we previously reported, EAT thickness was greater in patients with no-reflow (6.1 ± 2.1 vs. 3.9 ± 1.7 mm, p=0.001) and there was an inverse correlation between EAT thickness and STR (r=-0.414, p=0.001). EAT thickness was also significantly correlated with waist circumference (r=0.429, p=0.01). On the other hand, fasting blood glucose, triglyceride levels, HDL-C levels, hypertension, diabetes mellitus and metabolic syndrome did not differ significantly between groups (p>0.05). As expected, peak CK-MB levels were higher and left ventricular ejection fraction was significantly lower in the no-reflow group (203.1 ± 129.4 vs. 142.4 ± 88.1 IU/L, p=0.04; and 41.8 ± 7.1% vs. 50.1 ± 7.9%, p=0.001; respectively).

Clinical outcomes

Follow-up information was available for 102 (89%) of the 114 patients. The reasons for dropout were a change in telephone number (n=8) and non-cardiac death (n=4). Throughout the 3-year follow up, there were significantly more admissions for heart failure in the patients with no-reflow (n=5 [20%] vs. n=1 [1%], p= 0.003) (Table 2). However, there was no significant difference between patients with no-reflow and those without in terms of major adverse cardiac events, cardiac death, non-fatal myocardial infarction and target vessel revascularisation (p>0.05) (Figure 2). In the subgroup analysis, group I patients with no-reflow also showed a higher frequency of admission for heart failure (n=4 [44%] vs. n=1 [6%], p=0.04) (Table 3). In addition, in the subgroup analysis patients with no-reflow and a culprit lesion in the left anterior descending, circumflex or right coronary artery all showed more admissions for heart failure, but the differences were not significant (n=2 [17%] vs. n=0 [0%], p=0.09; n=1 [20%] vs. n=0 [0%], p=0.11; n=2 [25%] vs. n=1 [3%], p=0.07; respectively).

In addition, female patients had more admissions for heart failure (n=4 [26%] vs. n=2 [2%], p=0.004). Female patients demonstrated a trend towards increased body mass index (28.8 ± 3.9 vs. 27.3 ± 3.6 kg/m^2, p=0.16), age (57.3 ± 11.9 vs. 53.4 ± 11 years, p=0.20), fasting glucose (130.8 ± 38.7 vs. 120.9 ± 38.5 mg/dL, p=0.36) and symptom onset to balloon time (238.3 ± 99.3 vs. 185.4 ± 115.3 min, p=0.09).

Left ventricular ejection fraction determined within 72 hours of admission for STEMI was not sig-

Table 1. Clinical characteristics of the patients grouped according to ST-segment resolution.

	ECG findings		
	Normal reflow (n= 89)	No-reflow (n=25)	p
Age(y)	53.3 ± 10.3	55.8 ± 13.7	0.32
Sex (male/female)	79/10	20/5	0.25
Symptom-onset-to-balloon time (min)	194.4 ± 116.2	185 ± 96.4	0.71
Door-to-balloon time (min)	28.8 ± 8.1	30.8 ± 7.6	0.28
Incidence of pre-infarction angina (n [%])	33 [37]	6 [24]	0.22
Admission Killip class ≥2 (n [%])	4 [5]	1 [4]	0.99
Body mass index (kg/m^2)	27.1 ± 3.8	28.9 ± 2.7	0.03
Diabetes mellitus (n [%])	17 [19]	6 [24]	0.59
Smoking (n [%])	48 [54]	15 [60]	0.59
Systolic blood pressure (mmHg)	123.9 ± 39.7	128.2 ± 44.7	0.16
Diastolic blood pressure (mmHg)	73.9 ± 14.8	76.3 ± 16.2	0.35
Haemoglobin (mg/dL)	14.3 ± 1.6	13.5 ± 1.4	0.38
GFR (MDRD) (mL/min/1.73m^2)	101.5 ± 22.8	93.8 ± 28.3	0.17
Total cholesterol (mg/dL)	208.5 ± 32.6	213.7 ± 28.1	0.49
LDL-C (mg/dL)	124.3 ± 23.8	128.3 ± 20.5	0.49
Metabolic syndrome components:			
• Fasting glucose (mg/dL)	119.2 ± 38.5	132.9 ± 37.1	0.12
• HDL-C (mg/dL)	41.6 ± 7.9	40.1 ± 7.1	0.44
• Triglycerides (mg/dL)	199.8 ± 156.8	215.3 ± 126.8	0.66
• Waist circumference (cm)	96.6 ± 9.1	101.4 ± 10.2	0.03
• Hypertension (n [%])	29 [33]	11 [44]	0.29
Metabolic syndrome (n [%])	34 [38]	13 [52]	0.22
Anterior wall infarction (n [%])	30 [34]	12 [48]	0.19
Culprit lesion:			0.25
• LAD (n [%])	30 [34]	12 [48]	
• CX (n [%])	14 [16]	5 [20]	
• RCA (n [%])	45 [50]	8 [32]	
Peak creatine kinase-MB (IU/L)	142.4 ± 88.1	203.1 ± 129.4	0.04
LVEF (%)	50.1 ± 7.9	41.8 ± 7.1	0.001
Good collateral circulation (n [%])	39 [44]	8 [32]	0.29
Triple-vessel disease	15	28	0.12
Stent implantation (n [%])	76 [85]	24 [96]	0.15
Stent diameter (mm)	3.2 ± 0.4	3.2 ± 0.5	0.79
Stent length (mm)	19.3 ± 4.4	19.9 ± 4.9	0.51
Further stent implantation (n [%])	9 [10]	1 [4]	0.34
EAT thickness (mm)	3.9 ± 1.7	6.1 ± 2.1	0.001
Medication after infarction:			
• ACE inhibitor (n [%])	82 [92]	25 [100]	0.15
• β-blocker (n [%])	82 [92]	24 [96]	0.50
• GP IIb/IIIa receptor blocker (n [%])	57 [64]	15 [60]	0.71
• Statin (n [%])	87 [98]	25 [100]	0.45
• Nitrate (n [%])	50 [56]	16 [64]	0.48
STR (%)	74.2 ± 13.2	19.6 ± 14.8	0.001

ACE-I – angiotensin converting enzyme inhibitor; GFR (MDRD) – glomerular filtration rate (Modification of Diet in Renal Disease); GP IIb/IIIa – glycoprotein IIb/IIIa; HDL-C – high density lipoprotein-cholesterol; LAD – left anterior descending artery; LCX – left circumflex artery; LDL-C – low density lipoprotein-cholesterol; LVEF – left ventricular ejection fraction; RCA – right coronary artery; STR – ST-segment resolution.

nificantly lower than in patients with admission for heart failure (45.7 ± 8.2 vs. 48.6 ± 8.8%, p=0.44).

The effects of different variables on admission for heart failure were calculated in a separate univariate analysis for each. The variables for which the unadjusted p-value was <0.10 in logistic regression analysis were identified as potential risk markers and were included in the full model. Diabetes mellitus, CK-MB, female sex and no-reflow were analysed using a multivariate logistic regression model. The multivariate logistic regression analysis demonstrated that no-reflow and female sex independently predicted admission for heart failure (odds ratio, OR: 19.3, 95% confidence interval, CI: 1.4-269.7, p=0.03, and OR: 24.9, 95%CI: 2.2-288.8, p=0.01, respectively), whereas EAT thickness was not found be a predictor of ad-

Table 2. Major adverse cardiac events at 3-year follow up.

ECG findings	Normal reflow (n=77)	No-reflow (n=25)	p
Cardiac death (n [%])	5 [7]	2 [8]	0.99
Nonfatal MI (n [%])	12 [16]	7 [28]	0.17
Target-vessel revascularisation (n [%])	18 [23]	6 [24]	0.95
Admission for heart failure (n [%])	1 [1]	5 [20]	0.003
MACE (n [%])	23 [30]	12 [48]	0.1

MACE – major adverse cardiac events; MI – myocardial infarction.

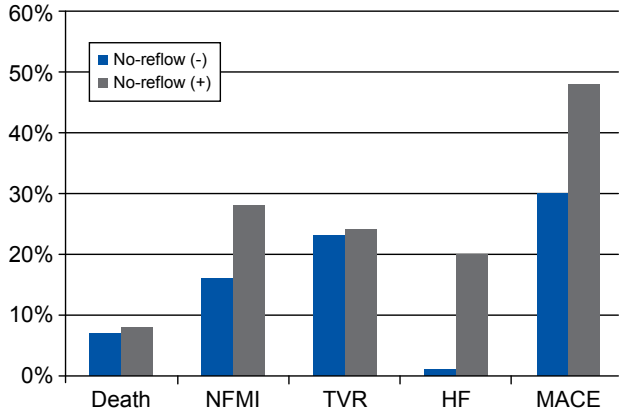

Figure 2. Box-plots indicating the clinical outcomes in no-reflow (+) and no-reflow (-) groups. HF – admission for heart failure; MACE – major adverse cardiac events; NFMI – non-fatal myocardial infarction; TVR – target vessel revascularisation.

mission for heart failure (Table 4). Receiver-operating characteristic curve analysis demonstrated good diagnostic accuracy for the percentage of persistent ST-segment elevation in predicting admission for heart failure (area under curve, AUC = 0.74, 95%CI: 0.54-0.95, p=0.048) (Figure 3).

Observer variability

The intra- and inter-observer variabilities for the measurements of STR and EAT thickness were 3.5% and 4.5%, and 4.2% and 5.4%, respectively.

Discussion

In the present study, admission for heart failure during the long-term follow up was revealed to be significantly more frequent in patients with no-reflow and in female patients. Although patients with no-reflow and lower EAT thickness showed a higher frequency of admission for heart failure in the subgroup analysis, the multivariate logistic regression analysis demonstrated that only no-reflow and female sex independently predicted admission for heart failure.

Previous studies have shown that no-reflow is strongly correlated with short- and long-term morbidity and mortality in acute myocardial infarction.[1,2,22] The relationship between the degree of ST-segment resolution, which has been well accepted as an ECG sign of myocardial reperfusion, and subsequent mortality from acute myocardial infarction was also found to be significant.[23] No-reflow is an independent predictor of an adverse clinical outcome after pPCI in STEMI, regardless of infarct size, and is associated with heart failure and increased mortality.[24] The presence and extent of no-reflow strongly predicts left ventricular remodel-

Table 3. Major adverse cardiac events at 3-year follow up in subgroups categorised according to EAT thickness.

ECG findings	Normal reflow (n=77)		p	No-reflow (n=25)		p
EAT thickness	Group I <5.1 mm (n=55)	Group II ≥5.1 mm (n=22)		Group I <5.1 mm (n=9)	Group II ≥5.1 mm (n=16)	
Cardiac death (n [%])	3 [6]	2 [9]	0.62	0 [0]	2 [13]	0.52
Nonfatal MI (n [%])	7 [13]	5 [23]	0.27	3 [33]	4 [25]	0.66
Target-vessel revascularisation (n [%])	12 [22]	6 [27]	0.61	4 [44]	2 [13]	0.07
Admission for heart failure (n [%])	1 [2]	0 [0]	0.99	4 [44]	1 [6]	0.04
MACE (n [%])	16 [29]	7 [32]	0.81	5 [56]	7 [44]	0.57

EAT – epicardial adipose tissue; MACE, major adverse cardiac events, MI, myocardial infarction.

Table 4. Effects of variables on admission for heart failure in univariate and multivariate logistic regression analyses.

	OR (95%CI)	p
Univariate predictors:		
Diabetes mellitus	4.3 (0.8-23.3)	0.09
Creatine kinase-MB	1.007 (1-1.01)	0.04
Female sex	15.5 (2.5-94.4)	0.003
No-reflow	19 (2.1-171.9)	0.009
Multivariate predictors:		
Female sex	24.9 (2.2-288.8)	0.01
No-reflow	19.3 (1.4-269.7)	0.03

CI – confidence interval; – odds ratio.

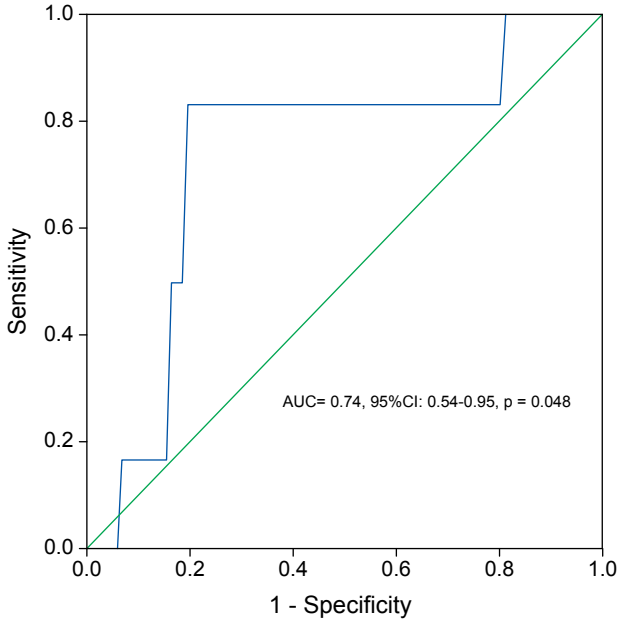

Figure 3. Receiver operating characteristic curve analysis of percentage persistent ST-segment elevation for predicting admission for heart failure. The analysis demonstrated good diagnostic accuracy for the percentage of persistent ST-segment elevation in predicting admission for heart failure (area under curve [AUC]=0.74, 95%CI: 0.54-0.95, p=0.048).

ling,[25] which is associated with a high risk of heart failure in post-MI patients and underlies the link between heart failure and MI.[26] In keeping with these previous studies, our findings also showed that no-reflow was associated with admission for heart failure after STEMI.

EAT has been demonstrated to have a significant correlation with metabolic risk factors such as waist circumference, blood pressure, fasting glucose, insulin resistance and hyperlipidaemia.[27,28] Consequently, EAT was recognised as a novel marker for cardiometabolic risk.[6,7] Our early previously published findings also revealed that EAT was significantly associated with waist circumference and no-reflow.[11] There are too few data to draw certain conclusions about the relationship of EAT to coronary atherosclerosis. The deleterious effect of EAT on the coronary arteries has been addressed in several articles. An association was suggested with coronary atherosclerosis[11,29-31] and depressed myocardial function.[32] However, it was postulated/shown that EAT might also exert a protective effect through the secretion of adiponectin and adrenomedullin, adipokines with anti-inflammatory properties in response to local or systemic metabolic or mechanical insults.[13] Microscopically, EAT is composed of adipocytes, stromovascular, inflammatory and immune cells.[12] Both adipocytes and tissue macrophages produce adipokines and cytokines. Adipokines with anti-inflammatory properties, adiponectin and adrenomedullin, and several pro-inflammatory cytokines, such as tumour necrosis factor-alpha, monocyte chemotactic factor-1, interleukin-1 beta, and interleukin-6, interact with coronary arteries and myocardium via two mechanisms (i.e. paracrine and vasocrine).[12] Furthermore, there are conflicting data regarding the role of EAT in the development of major adverse cardiac events. Shmilovich et al postulated that EAT might be associated with major adverse cardiac events.[14] In contrast, Albuquerque et al showed that EAT, as measured using echocardiography, does not strongly predict major adverse cardiac events.[33] In our study, EAT thickness was not determined to be a predictor of clinical outcomes in patients with acute STEMI undergoing pPCI.

Some previous studies reported higher mortality rates after STEMI in women, whereas others found no sex-related differences in mortality, especially after adjustment for age and other prognostic factors.[34-37] It was reported that women had a higher baseline risk profile than did men. Women as a group are older, with more comorbidities, and also have significantly longer pain-to-balloon times compared with men.[38] Although we found that female patients had higher baseline risk factors, female sex was determined to be an independent predictor for admission for heart failure.

Study limitations

This study had several limitations. First, the major limitation of this study is its small sample size. Therefore further studies will be needed to provide more

precise data regarding the role of EAT in the development of major adverse cardiac events in STEMI patients. Second, although quantitative myocardial contrast echocardiography or myocardial blush grading can give more information about myocardial reperfusion, an indirect method, STR, was used. Third, although echocardiography is more practical and sufficiently reliable, magnetic resonance imaging is currently the gold standard diagnostic method for measuring epicardial fat thickness. Fourth, LV diastolic function was not evaluated and left ventricular function was not serially evaluated by echocardiography in the follow up. Finally, the association between EAT and the no-reflow phenomenon, which was defined in our previous study, might not be strong enough to display EAT as a predictive factor for clinical outcomes after STEMI.

Conclusion

These results suggest that the no-reflow phenomenon, together with female sex, are independent predictors of admission for heart failure in the long-term follow up of patients with STEMI who have undergone pPCI. Therefore, patients with these risk factors should be carefully evaluated and closely followed for potential adverse cardiac events.

Although increased EAT thickness might be correlated with no-reflow in STEMI, in the light of our present findings it is not possible to state that EAT thickness is associated with clinical outcomes after acute STEMI.

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