

Predictors and prognosis for incident in-hospital heart failure in patients with preserved ejection fraction after first acute myocardial infarction

An observational study

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Abstract

Patients with acute myocardial infarction (AMI) complicated by heart failure with preserved ejection fraction (HFpEF) are likely to have more adverse cardiovascular events and higher mortality. The purpose of this study was to examine the predictors and outcomes in AMI patients complicated by HFpEF.

We examined the demographics, clinical data, and clinical outcomes in 405 consecutive subjects who firstly presented with AMI after undergoing emergency percutaneous coronary intervention from January 2013 to June 2016.

Three hundred twenty patients and eighty-five patients were classified into the nonheart failure (non-HF) group and HFpEF group, respectively. Patients with HFpEF had higher prevalence of prior hypertension, had higher levels of biomarkers, and had a larger left atrial diameter with a nondilated left ventricle were more likely to develop multivessel disease-vessels and had infarction-related artery located in left anterior descending artery than patients without HF. Moreover, patients with HFpEF had a higher probability of developing the in-hospital incident cardiovascular complications and death than non-HF patients.

Two routine biomarkers, levels of hypersensitive C-reactive protein and N-terminal-pro brain natriuretic peptide, and number of diseased-vessels were independent predictors for in-hospital HFpEF incidence in AMI patients with preserved LVEF. AMI patients with HFpEF had a higher probability of in-hospital cardiovascular outcomes and mortality.

Abbreviations: ALT = alanine aminotransferase, AMI = acute myocardial infarction, AST = aspartate transaminase, CI = confidence interval, CK-MB = MB isoenzyme of creatine kinase, DBP = diastolic blood pressure, HDL-C = high-density lipoprotein cholesterol, HF = heart failure, HFpEF = heart failure with preserved ejection fraction, HR = heart rate, Hs-CRP = hypersensitive C-reactive protein, IRA = infarction-related artery, LAD = left anterior descending artery, LAd = left atrium diameter, LCX = left circumflex artery, LDL-C = low-density lipoprotein cholesterol, LM = left main, LVEDd = left ventricular end-diastolic dimensions, LVEF = left ventricular ejection fraction, LVESd = left ventricular end-systolic dimensions, NT-proBNP = N-terminal-pro brain natriuretic peptide, OR = odds ratio, PCI = percutaneous coronary intervention, PDW = platelet distribution width, ROC = receiver operating characteristic, SBP = systolic blood pressure, Scr = serum creatinine, TB = total bilirubin, VT/VF = ventricular tachycardia/fibrillation, WBC = white blood cell.

Keywords: acute myocardial infarction, cardiovascular event, heart failure with preserved ejection fraction, predictor, risk factor

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1. Introduction

Heart failure (HF) with preserved ejection fraction (HFpEF) is increasingly being recognized as a major public health problem accountable for nearly 50% of all HF cases. The 2-year mortality is up to 26.6% in Asians complicating HFpEF.^[1] Acute myocardial infarction (AMI) is one of the main causes of morbidity and in-hospital mortality worldwide, although the increasing use of early myocardial reperfusion and medical treatments have contributed significantly to the decline in mortality.^[2-4] In AMI patients, the presence of HFpEF might worsen the prognosis, and the incident adverse events increase due to the therapeutic limitations.^[3,4] Timely evaluation of HFpEF would be useful for risk stratification in patients after an attack of AMI.

Previous studies have identified several risk factors for the development of post-AMI HF, such as advancing age, coexistence of previous coronary disease, infarction size, multivessel coronary disease, reperfusion efficiency, and other concomitant medical conditions^[5,6]; however, these studies did not differentiate between HFpEF and HF with reduced ejection fraction, or

classified them by the in-hospital Killip score at admission.^[7] Data pertaining to the prevalence of HFpEF in AMI patients are highly limited especially in Asia. Several clinical studies on post-AMI diastolic dysfunction have established the diagnosis of HFpEF using the clinical HF symptoms; few clinical studies have focused on the predictive factors and prognosis of patients with HFpEF following AMI, especially after primary percutaneous coronary intervention (PCI). Further, homologous left ventricular ejection fraction (LVEF) cut-off points have also been used to establish a diagnosis of HFpEF.^[8–10] Notably, it has been demonstrated by another study that the prevalence for HFpEF in AMI patients has remained stable despite the declining of prevalence HF with reduced LVEF in post-AMI patients.^[11] Therefore, we aimed to early identify HFpEF patients in patients after AMI with normal LVEF value, and evaluate the predictors, prognosis of patients with HFpEF after AMI by analyzing clinical characteristics, biomarkers, angiographic course, medical treatments, and clinical outcomes.

2. Materials and methods

2.1. Study population

The procedures in this study complied with the Declaration of the Helsinki, and the study protocol was approved by the Ethics Committee of the local institution (The First Affiliated Hospital of Soochow University). Our study was registered at ClinicalTrials.gov with clinicalTrials.gov ID NCT03351179. In this single-center observational study, we retrospectively evaluated 705 consecutive patients with first incident AMI treated with primary PCI in the cardiac intensive care unit of our hospital from January 2013 to June 2016. The diagnosis of AMI was based on the presence of a typical chest pain history, electrocardiographic changes, an increase in the serum cardiac biomarkers, and results of coronary angiography.^[12,13] The definition of HFpEF was established in accordance with the latest published guidelines.^[14] HFpEF diagnosis was established in AMI patients with typical symptoms or signs of HF, LVEF ≥ 0.5 which is measured with M-mode method, or other evidences of diastolic dysfunction to diagnose HFpEF of echocardiography measurements, but not accompanied by any evidence of reduced systolic function, as evaluated using echocardiography. The HFpEF diagnosis was also referred to the Killip grade and N-terminal-pro brain natriuretic peptide (NT-proBNP) level. Exclusion criteria were severe inflammatory diseases, valvular heart disease, noncardiac cause symptoms, serious hepatic and renal failure, congenital cardiomyopathy, and pericardial diseases.

2.2. Data collection

We collected data pertaining to demographic characteristics (age and sex), previous history, and risk factors of AMI (hypertension, hyperlipidemia, diabetes mellitus, smoking, and stroke), biomarkers, echocardiographic measurements, clinical characteristics, medical procedures and treatments, as well as in-hospital complications. Laboratory biomarkers, including white blood cells (WBCs), neutrophils, hemoglobin, red blood cell distribution width, hematocrit, platelet distribution width (PDW), platelet count, total bilirubin (TB), alanine aminotransferase (ALT), aspartate transaminase (AST), total protein, albumin, hypersensitive C-reactive protein (Hs-CRP), uric acid, serum creatinine (Scr), glucose, triglyceride, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein

cholesterol (LDL-C), apolipoprotein A, apolipoprotein B, lipoprotein (a), and NT-proBNP, were measured during first 24 h. Peak levels of MB isoenzyme of creatine kinase (CK-MB) and cardiac troponin I were measured. Clinical characteristics included heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP). Echocardiographic data comprised the left atrium diameter (LAd), left ventricular end-systolic dimensions (LVESd), and left ventricular end-diastolic dimensions (LVEDd) on admission. Each enrolled subject was undergoing PCI therapy and appropriated prescriptions. The associated coronary pathological changes, medical therapy, in-hospital complications (severe sinus bradycardia or sinus arrest, acute attack of atrial fibrillation/flutter, malignant ventricular tachycardia/fibrillation [VT/VF], and acute attack of severe HF), length of hospital stay, and death evaluated in the current study. Finally, the variables related to incident HFpEF in AMI patients were analyzed using univariate logistic regression analyses and multivariate logistic regression analyses to identify the independent predictors.

2.3. Statistical analyses

All data were analyzed using the SPSS software package (version 17.0, SPSS, Chicago, IL). Continuous variables are presented as mean \pm standard deviation or median (range) values and were compared using the independent-sample *t* test (data with normal distribution) or Mann–Whitney *U* test (data with non-normal distribution). Categorical variables are expressed by numbers (percentage) of patients in each group and then were analyzed using the chi-squared or Fisher exact test. The independent predictors for HFpEF in AMI patients were identified by conducting stepwise multivariate logistic regression analyses of various variables confirmed using univariate logistic regression analyses. A receiver operating characteristic (ROC) curve was constructed to assess the predicted probability based on the logistic model. $P < .05$ (2-sided) was considered statistically significant.

3. Results

The entire study population consisted of 705 first incident AMI patients undergoing primary PCI, 279 of these patients were excluded owing to an LVEF value <0.5 . The remaining 426 patients were included and divided into the HFpEF and non-HF groups; of these, 15 patients of the non-HF group and 6 patients of the HFpEF group were excluded because of death on the operating-table, incomplete data, or other exclusion criteria. Finally, the study was conducted on 320 patients in the non-HF group and 85 patients in the HFpEF group. First, the clinical characteristics, biomarkers, and echocardiological data of the 2 groups were compared and had been summarized in Table 1. AMI patients with HFpEF had higher prevalence of prior history of hypertension, markedly increased levels of WBCs, neutrophils, TB, ALT, AST, total protein, Hs-CRP, Scr, glucose, NT-proBNP, peak CK-MB value, and peak troponin I, and had significant decreased level of DBP than those without HF. Moreover, patients with AMI and HFpEF had larger LAd, LVESd, and LVEDd than those without HF. There were some nonsignificant differences with regard to age; the sex distribution; previous history except prior hypertension; hemoglobin level; red blood cell distribution width; hematocrit; PDW; platelet count; level of albumin, uric acid, TG, TC, HDL-C, LDL-C, apolipoprotein A, apolipoprotein B, and lipoprotein (a); HR; and SBP between the 2 groups.

Table 1
Baseline characteristics, biomarkers, and echocardiological measurements of study subjects.

Variables	HFpEF group (n=85)	Non-HF group (n=320)	P
Age, y	60.38 ± 14.65	61.60 ± 13.00	.638
Sex, male, n (%)	72 (84.70)	279 (87.19)	.550
Sex, female, n (%)	13 (17.65)	41 (12.81)	.550
Prior hypertension, n (%)	63 (74.12)	165 (51.56)	.000
Prior hyperlipidemia, n (%)	6 (7.06)	28 (8.75)	.617
Prior diabetes mellitus, n (%)	19 (22.35)	66 (20.63)	.728
Prior stroke, n (%)	3 (3.53)	10 (3.13)	.740
Smoking, n (%)	57 (67.06)	215 (67.19)	.982
Laboratory biomarkers			
White blood cell count, ×10 ¹² /L	11.91 ± 3.82	11.04 ± 3.21	.035
Neutrophil count, ×10 ¹² /L	9.61 ± 3.74	8.39 ± 3.08	.007
Hemoglobin, g/dL	143.08 ± 20.67	143.66 ± 17.64	.609
Red blood cell distribution width, fL	13.07 ± 0.78	13.14 ± 0.80	.503
Hematocrit	0.41 ± 0.07	0.43 ± 0.08	.160
Platelet distribution width, fL	16.20 (16.00–16.40)	16.20 (15.90–16.50)	.830
platelet count, ×10 ⁹ /L	212.08 ± 67.49	211.12 ± 69.93	.618
Total bilirubin, μmol/L	17.60 (14.80–21.95)	15.30 (12.13–20.00)	.001
Alanine aminotransferase, U/L	48.00 (34.00–72.00)	42.00 (28.00–60.75)	.030
Aspartate transaminase, U/L	248.73 ± 148.09	185.50 (97.00–311.75)	.013
Total protein, g/L	65.10 ± 5.78	40.49 ± 5.08	.028
Albumin, g/L	40.42 ± 5.20	40.49 ± 5.08	.919
Hs-CRP, mg/L	10.77 (4.19–12.97)	4.64 (2.12–10.50)	.000
Serum uric acid, μmol/L	375.08 ± 136.99	346.45 ± 106.75	.040
Serum creatinine, mg/dL	0.87 (0.73–1.15)	0.87 (0.70–0.95)	.021
eGFR, mL/min per 1.732 m ²	91.92 ± 37.28	101.09 ± 29.08	.016
Glucose, mmol/L	6.06 (5.14–8.22)	5.62 (4.85–6.68)	.014
Total cholesterol, μmol/L	4.46 ± 1.16	4.57 ± 1.00	.374
Triglyceride, μmol/L	1.22 (0.94–1.77)	1.35 (0.90–2.07)	.383
HDL-C, μmol/L	1.04 ± 0.24	1.06 ± 0.21	.266
LDL-C, μmol/L	2.77 ± 0.92	2.92 ± 0.90	.108
Apolipoprotein A, mg/L	1.21 ± 0.18	1.23 ± 0.17	.288
Apolipoprotein B, mg/L	0.98 ± 0.23	1.01 ± 0.23	.282
Lipoprotein (a), mg/L	88.00 (36.00–205.00)	86.00 (40.00–149.00)	.490
NT-proBNP, pg/mL	1835.00 (1140.00–3144.50)	359.90 (178.6–624.00)	.000
Peak CKMB, μg/L	209.84 ± 146.07	134.32 (67.5–263.41)	.002
Peak troponin I, μg/L	49.10 (13.05–80.00)	27.00 (9.59–77.25)	.030
Heart rates, beats/min	79.67 ± 17.24	77.29 ± 13.28	.170
Systolic blood pressure, mm Hg	125.31 ± 31.29	126.20 ± 20.04	.802
Diastolic blood pressure, mm Hg	77.08 ± 15.46	77.16 ± 13.60	.020
Echocardiogram findings on admission			
LAd, mm	38.70 ± 5.29	37.18 ± 4.70	.036
LVESd, mm	35.65 ± 6.42	34.20 ± 4.67	.020
LVEDd, mm	51.42 ± 5.25	49.87 ± 4.61	.008

CKMB = MB isoenzyme of creatine kinase, eGFR = estimated glomerular filtration rate, HDL-C = high-density lipoprotein cholesterol, HF = heart failure, HFpEF = heart failure with preserved ejection fraction, Hs-CRP = hypersensitive C reactive protein, LAd = left atrial diameter, LDL-C = low-density lipoprotein cholesterol, LVEDd = left ventricular end-diastolic dimension, LVESd = left ventricular end-systolic dimension, N-terminal proBNP = NT-proBNP.

*P < .05 (HFpEF group vs non-HF group).

Thereafter, further comparisons of the angiographic findings and medical procedures were conducted between the 2 groups (Table 2). A longer length of attack to reperfusion was found in AMI patients with HFpEF than the other group. There was considerable difference in the relative number of disease-vessels and distribution in the location of infarction-related artery (IRA) between the groups. Significantly higher number of patients in the HFpEF had multiple disease-vessels (25 [29.41%] vs 42 [13.13%]), and a notable increased proportion of coronary IRA located in left anterior descending artery (LAD) (52 [61.18%] vs 129 [40.31%]) than those in the non-HF group, while a significantly lower number of these patients had single disease-vessel (41 [48.24%] vs 195 [60.94%]) and IRA located in right coronary artery (29 [34.12%] vs 151[47.19%]) (Table 2).

Moreover, AMI patients with HFpEF were more likely to receive angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers, beta-blockers, aldosterone antagonists than those without HF; by contrast, no significant difference was observed with respect to the adherence to therapeutic intravenous injection of glycoprotein IIb/IIIa inhibitors and oral usage of antiplatelet, statins between the groups. In addition to the above parameters, relative number of 2 disease-vessels; relative number of 1, 2, multiple IRA; relative number of IRA located in the left main (LM) or left circumflex artery (LCX); relative number of thrombolysis in myocardial infarction flow grade after PCI; and the utilization rate of thrombus aspiration catheter and intra-aortic balloon pump showed no statistical differences between the 2 groups.

Table 2

In-hospital angiographic characteristics and other medical procedures.

Variables	HFpEF group (n = 85)	Non-HF group (n = 320)	P
Length from attack to reperfusion, h	7 (5.1–10.25)*	6 (4.43–8.32)	.002
Number of disease-vessels, n (%)			.002
One	41 (48.24)	195 (60.94)	
Two	19 (22.35)	83 (26.56)	
Multiple	25 (29.41)	42 (13.13)	
Number of infarction-related artery, n (%)			.229
One	75 (88.24)	297 (92.81)	
Two	8 (9.41)	21 (24.71)	
Multiple	2 (2.35)	2 (0.63)	
Location of infarction-related artery, n (%)			.016
LM	3 (3.53)	4 (1.25)	
LAD	52 (61.18)	129 (40.31)	
LCX	15 (17.65)	62 (19.38)	
RCA	29 (34.12)	151 (47.19)	
TIMI flow grade after PCI, n (%)			.639
0–1	1 (1.18)	2 (1.75)	
2	7 (8.24)	36 (10.92)	
3	77 (90.59)	282 (87.34)	
Thrombus aspiration catheter, n (%)	4 (4.71)	36 (11.25)	.072
Intra-aortic balloon pump, n (%)	2 (2.35)	3 (0.94)	.619
Glycoprotein IIb/IIIa inhibitors (IV), n (%)	52 (61.18)	180 (56.25)	.414
Antiplatelet, n (%)	84 (98.82)	318 (99.38)	.508
Statins, n (%)	85 (100)	317 (99.06)	.624
ACEI or ARB, n (%)	66 (77.65)*	183 (57.19)	.001
Beta-blockers, n (%)	74 (87.06)*	221 (69.06)	.001
Aldosterone antagonist, n (%)	23 (27.06)*	40 (12.50)	.001

Disease-vessels were defined as ≥50% diameter stenosis in major epicardial branches (LAD, LCX, RCA).

ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin-receptor blocker, HF = heart failure, HFpEF = heart failure with preserved ejection fraction, LAD = left anterior descending artery, LCX = left circumflex artery, LM = left main, PCI = percutaneous coronary intervention, RCA = right coronary artery, TIMI = thrombolysis in myocardial infarction.

* P < .05 (HFpEF group vs non-HF group).

Data regarding the incidence of cardiovascular complications and prognosis are presented in Table 3. We found that the incidence of paroxysmal atrial fibrillation/flutter was significantly higher in AMI patients with HFpEF than in those without HF. In addition, we found that higher probability of the incidence of severe sinus bradycardia or sinus arrest, malignant VT/VF, length of hospital stay, and number of death in hospital in HFpEF group, though no significant difference, compared to patients in the non-HF group in this study.

In the univariate logistic regression analyses, levels of WBC counts; neutrophil counts; TB; AST; Hs-CRP; Scr; NT-proBNP; peak troponin I; LAd; LVESd; LVEDd; number of disease-vessels; and patients with prior hypertension predicted the incidence of HFpEF in the AMI patients (Table 4). The stepwise multivariate logistic regression analysis adjusted for these variables demonstrated that Hs-CRP (odds ratio [OR]: 1.248; 95% confidence interval [CI]: 1.031–1.511; P = .023), NT-proBNP (OR: 1.005; 95% CI: 1.003–1.008; P = .000), and number of disease-vessels

(OR: 4.108; 95% CI: 1.595–10.578; P = .003) were independently correlated with the occurrence of HFpEF in AMI patients (Table 4). The area of the ROC curve of the NT-proBNP, Hs-CRP, and number of disease-vessels were 0.959 (95% CI: 0.934–0.983, P = .000), 0.705 (95% CI: 0.630–0.779 P = .000), and 0.589 (95% CI: 0.506–0.673, P = .039), respectively, suggesting the predictive effect on the risk of HFpEF in AMI patients (Fig. 1).

4. Discussion

In the present study, AMI patients with HFpEF had features of higher prevalence of prior hypertension; higher levels of WBC counts, neutrophils counts, TB, ALT, AST, total protein, Hs-CRP, Scr, blood glucose, NT-proBNP, peak CK-MB, and troponin I; and larger LAd, LVESd, and LVEDd than those without HF. In addition, AMI patients with HFpEF had longer length of attack to reperfusion, were more likely to have multiple diseased-vessels and IRA located in the LAD than AMI patients

Table 3

In-hospital adverse events as a function of acute myocardial infarction in HFpEF group and non-HF group.

Variables	HFpEF group (n = 85)	Non-HF group (n = 320)	P
Severe sinus bradycardia or sinus arrest, n (%)	7 (8.24)	29 (9.06)	.812
Paroxysmal atrial fibrillation/flutter, n (%)	8 (9.41)	6 (1.88)	.002
Malignant ventricular tachycardia/fibrillation, n (%)	5 (5.88)	13 (4.06)	.669
Length of hospital stay, d	8 (7–10.5)	7 (6–9)	.070
Death in hospital, n (%)	3 (3.53)	9 (2.81)	.729

HF = heart failure, HFpEF = heart failure with preserved ejection fraction.

* P < 0.05 (HFpEF group vs non-HF group).

Table 4
Univariate and multivariate logistic regression analyses for predictors of hospitalized HFpEF in post-AMI patients.

Variables	Univariate logistic regression			Multivariate logistic regression		
	OR	95% CI	P	OR	95% CI	P
White blood cell counts	1.077	1.005–1.155	.036	1.308	0.831–2.059	.246
Neutrophil counts	1.119	1.039–1.205	.033	0.849	0.555–1.300	.452
Total bilirubin	1.030	1.003–1.058	.031	1.041	0.943–1.148	.427
Alanine aminotransferase	1.005	0.998–1.013	.165			
Aspartate transaminase	1.002	1.000–1.004	.020	1.001	0.996–1.007	.697
Total protein	1.033	0.992–1.075	.116			
Hs-CRP	1.143	1.082–1.208	.000	1.248	1.031–1.511	.023
Serum creatinine	2.939	1.462–5.906	.002	0.651	0.151–2.808	.565
Glucose	1.070	0.999–1.145	.053			
NT-proBNP	1.011	1.002–1.020	.013	1.005	1.003–1.008	.000
Peak troponin I	1.020	1.002–1.011	.013	0.988	0.962–1.014	.345
Peak CKMB	1.001	1.000–1.003	.150			
Diastolic blood pressure	1.000	0.993–1.017	.965			
LAd	1.067	1.015–1.121	.011	0.972	0.834–1.133	.716
LVESd	1.060	1.009–1.113	.021	1.002	0.844–1.189	.985
LVEDd	1.071	1.018–1.127	.008	1.134	0.890–1.445	.309
Length (attack to reperfusion)	1.016	0.985–1.047	.317			
Number of disease-vessels	1.607	1.190–2.170	.002	4.108	1.595–10.578	.003
Prior hypertension	2.690	1.579–4.582	.000	1.807	0.434–7.523	.416

AMI = acute myocardial infarction, CI = confidence interval, CKMB = MB isoenzyme of creatine kinase, HFpEF = heart failure with preserved ejection fraction, Hs-CRP = hypersensitive C reactive protein, LAd = left atrial diameter, LVEDd = left ventricular end-diastolic dimension, LVESd = left ventricular end-systolic dimension, NT-proBNP = N-terminal-pro brain natriuretic peptide, OR = odds ratio.

without HF. Moreover, AMI patients with HFpEF had higher in-hospital paroxysmal atrial fibrillation/flutter than non-HF patients. It is noteworthy that in the present study, the Hs-CRP, NT-proBNP, and number of diseased-vessels were important independent predictors of the HFpEF course in AMI patients after PCI who have preserved LVEF. Moreover, AMI patients with HFpEF had higher incidence of paroxysmal atrial fibrillation/flutter and higher probability of risk in other cardiovascular outcomes and death by comparison with patients in the non-HF group.

The occurrence of HFpEF in post-AMI patients is a complex process. On one hand, ischemic and necrotic myocardium promotes the process of cardiac systolic and/or diastolic dysfunction. On the other hand, a stunned or hibernating myocardium in surrounding the surviving cardiomyocytes can present transient impairment of contraction and relaxation,^[15] especially affecting the diastolic function because ventricular diastole is an active process that requires consuming oxygen and glucose.^[16] Several studies have investigated the potential risk factors for incident HFpEF in AMI patients. Some investigators have reported that laboratory examinations also provide information regarding incident and prognostic HFpEF in AMI patients. High CRP levels and increased WBC counts and neutrophils counts are considered to be strongly and independently associated with the development of HF in atherosclerosis and have related to adverse effects in the myocardium.^[17–19] Acute hyperglycemia is frequently observed as transient increases in response to stressful conditions and critical illnesses, and appears to be an independent predictor of in-hospital outcomes in AMI.^[20,21] Liver abnormalities can be assessed by measuring the levels of parameters such as bilirubin, ALT, and AST. Accurate identification of liver abnormalities cannot only reflect non-hepatic diseases, and influence diagnostic as well as therapeutic processes, but also indicate the infarct size and thrombus burden, and enable the prediction of prognosis and mortality in AMI patients and in HF patients.^[21–26] Prior studies had also suggested that elevations in the CK-MB and troponin I levels were widely accepted as indicators of myocardial necrosis and as risk factors for the development of a fulminant course, and were useful in the diagnosis, risk stratification, guiding treatments, and provide prognostic information in patients with AMI.^[12,13,27] Consistent with these findings, AMI patients presenting with HFpEF in our study had higher levels of inflammatory indicators (WBC counts, neutrophils counts, and Hs-CRP), elevated level of blood glucose, liver biomarkers (TB, ALT, and AST), and myocardial necrosis indicators (CK-MB, troponin I) than non-

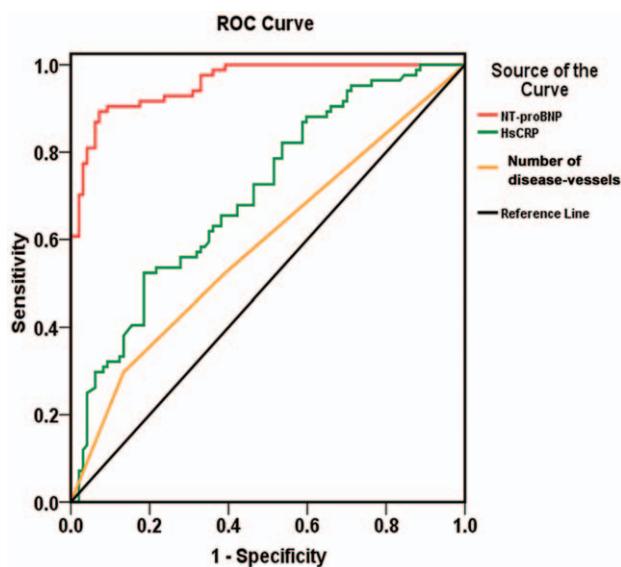


Figure 1. Receiver operating characteristic (ROC) curve of NT-proBNP, Hs-CRP, and number of disease-vessels for predicting the incidence of HFpEF in patients with acute myocardial infarction. Hs-CRP = hypersensitive C-reactive protein, NT-proBNP = N-terminal-pro brain natriuretic peptide.

HF patients. In addition, echocardiographic parameters such as a nondilated left ventricle and an increased left atrial size could aid the diagnosis and assessment of left ventricular diastolic dysfunction.^[14] The occurrence of HFpEF in AMI patients is significantly influenced by the coronary artery findings. In the present study, patients with HFpEF in AMI patients are more likely to have multiple disease-vessels and IRA located in LAD, and therefore the revascularization of disease-vessel and infarction-related LAD might be plays a protective role for the restoration of cardiac function.^[28]

It is noteworthy that level of Hs-CRP, NT-proBNP, and number of diseased-vessels have been proposed as independent predictors of HFpEF incidence in AMI patients; this was examined using multivariate logistic regression analyses. The development and progression of HFpEF involve multiple aspects. Considerable evidence exists to indicate that CRP is increased in response to the pathophysiological processes and can impair endothelial cells and stimulate cytokine production.^[29] The increased CRP levels in AMI patients may reflect the magnitude of the response to ischemic myocardial injury and myocardial necrosis, the severity of myocytes loss, ventricular remodeling, and prognosis in patients with AMI or cardiac failure.^[30–34] Previous studies had demonstrated that NT-proBNP level could predict adverse cardiovascular outcomes, cardiovascular morbidity and mortality in patients with ventricular dysfunction, as natriuretic peptides are secreted from the ventricle in response to wall stress, adverse hemodynamic alterations, and vascular dysfunction. Importantly, by examining the independent association of risk factors with HFpEF occurrence in AMI patients, our results had been noted that elevated NT-proBNP level predicts incident in-hospital HFpEF strongly in patients after AMI.^[35–38] Beyond above the routine use of above biomarkers for predictive purposes about incident HFpEF in AMI patients with preserved LVEF, number of disease-vessels could be recommended as an another independent contributor to HFpEF incidence in AMI patients in this study. Coronary characteristics of multiple disease-vessels indicate a large atherosclerotic burden, and are closely related to micro-embolization in the IRA that can potentially diminish myocardial perfusion and impair microcirculation.^[30,39] Furthermore, patients with multiple disease-vessels disease may have previous chronic myocardial ischemic injury, adverse ventricular remodeling, and poor tolerance to AMI injury.

5. Study limitations

Our study has certain limitations. First, this was a retrospective single-center observational study with a relatively small sample size. Second, the diagnosis of HFpEF is challenging. The study used LVEF $\geq 50\%$ as the threshold for diagnosing HFpEF; however, some patients did not have a completely normal EF accompanied by the absence of any symptoms and signs of reduced systolic function. These patients were not diagnosed with HFpEF in the current study. Third, echocardiographic measurements (such as E/A ratio and E/e' ratio) related to diastolic function upon admission was available. Finally, the exact score of the severity of coronary lesion stenosis was not analyzed.

6. Conclusions

This study showed that older age; higher WBC and neutrophil counts; elevated levels of TB, ALT, AST, Hs-CRP, blood glucose, CK-MB, and troponin I; LAD; multiple

diseased-vessels; and LAD-IRA are potential risk factors of incident HFpEF in first incident AMI patients with preserved LVEF who were undergoing primary PCI. Moreover, patients with HFpEF after AMI had a probably higher risk of in-hospital mortality and clinical complications. The Hs-CRP, NT-proBNP, and number of diseased-vessels were independent risk factors associated with HFpEF in first incident AMI patients. These findings can help clinicians perform prevention treatments for high-risk HFpEF incidence in patients with preserved LVEF who had higher levels of Hs-CRP and NT-proBNP, and multivessel of diseased-vessels.

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