Journal of Cardiothoracic Surgery

RESEARCH

Open Access

The diagnostic and prognostic value of serum miR-199a-5p combined with echocardiography in acute myocardial infarction

Lixin Xu[1], Jianfeng Lin[2*], Jianke Xia[1], Deng Chen[1] and Guohan He[1]

Abstract

Background Diagnosis and prognostic evaluation of acute myocardial infarction (AMI) are crucial for patients.

Objective The clinical significance of serum miR-199a-5p combined with echocardiography in AMI was investigated to provide some reference for clinical treatment.

Methods The study subjects were 90 AMI patients and 50 acute chest pain patients (control). All patients were examined by echocardiography and recorded LVEDV, LVESV, and LVEF. RT-qPCR was performed to detect the serum miR-199a-5p level. Pearson analysis was used to analyze the correlation of miR-199a-5p with LVEF and cTnI. The diagnostic value of miR-199a-5p combined with LVEDV, LVESV, and LVEF was assessed by the ROC curve. The occurrence of major adverse cardiovascular events (MACE) was recorded to analyze the prognostic value of miR-199a-5p by the Kaplan-Meier curve and Cox regression.

Results Serum miR-199a-5p was elevated in AMI, positively correlated with cTnI and negatively correlated with LVEF. The combination of miR-199a-5p with LVEDV, LVESV, and LVEF enhanced the sensitivity and specificity for the diagnosis of AMI. Patients with high miR-199a-5p expression were more likely to develop MACE. The combination of miR-199a-5p with LVEF improved the prediction of MACE.

Conclusions The combination of miR-199a-5p with echocardiography improved the diagnostic efficiency of AMI and provided prognostic information.

Keywords AMI, miR-199a-5p, Echocardiography, Diagnosis, MACE

*Correspondence:
Jianfeng Lin
wzts9099@163.com
[1]Department of Ultrasound, Wenzhou Third Clinical Institute Affiliated to Wenzhou Medical University, Wenzhou People's Hospital, Third Affiliated Hospital of Shanghai University, Wenzhou City, Zhejiang Province 325000, China
[2]Department of Cardiology, Wenzhou Third Clinical Institute Affiliated to Wenzhou Medical University, Wenzhou People's Hospital, Third Affiliated Hospital of Shanghai University, No. 299, Gu'an Road, Ouhai District, Wenzhou, Zhejiang 325000, China

Introduction

Acute myocardial infarction (AMI) is induced by insufficient blood and oxygen supply to the myocardium due to severe stenosis or occlusion of coronary arteries, resulting in necrosis of myocardial cells [1, 2]. AMI is characterized by a rapid onset and progression of the disease, as well as a high mortality rate [3]. Therefore, early diagnosis and treatment of AMI are essential to improve the prognosis and reduce the mortality of patients. Myocardial infarction is diagnosed and evaluated by clinical symptoms, dynamic changes of electrocardiogram, and markers of myocardial necrosis [4, 5]. Although troponin has high sensitivity in diagnosing AMI, it is also elevated in certain conditions such as renal failure, severe infections, and heart failure, thus resulting in a less specific diagnosis. Furthermore, recurrent infarction in patients who have recently experienced a myocardial infarction cannot be diagnosed by troponin [6, 7]. For the early diagnosis of AMI, the search for new biomarkers that are more sensitive and specific would be of great interest.

Echocardiography is a noninvasive imaging test, which can be used as a differential diagnostic method for early cardiac diseases, such as the evaluation of ventricular function and the degree of myocardial wall damage in ischemic areas [8]. Echocardiography is able to detect ventricular wall activity, especially to determine the local ventricular wall motion abnormality under load conditions, which can indirectly estimate myocardial ischemia, but this technique has a certain degree of timeliness, lower accuracy and sensitivity. Parameters obtained by echocardiography can visualize the state of cardiac function and further provide a reference for the prognosis of AMI [9, 10]. However, echocardiography may not easily detect coronary artery obstruction early in AMI patients, so a combination of other tests is necessary to diagnose AMI and assess the patient's condition.

Studies have suggested that microRNAs (miRNAs) are promising biomarkers for the diagnosis of AMI and have important clinical implications [11]. For example, abnormal expression of plasma miR-122-5p and miR-22-5p was found to better differentiate AMI patients from healthy controls [12]. In addition, previous studies have shown that miR-186-5p was associated with the prognosis of AMI patients and predicted the risk of developing major adverse cardiovascular events (MACE) [13]. Recent findings have revealed new insights into the role of miR-199a-5p in the pathogenesis of cardiovascular diseases. miR-199a-5p has been shown to play a pivotal role in the development of atherosclerosis and primary hypertension [14, 15]. Additionally, miR-199a-5p has been identified as a key regulator of myocardial ischemia/reperfusion (I/R) induced myocardial injury [16]. Therefore, it is hypothesized that miR-199a-5p has potential clinical significance in AMI.

In light of the above, the present study sought to observe the changes in echocardiographic indexes and serum miR-199a-5p levels in AMI patients, and to explore their value in the diagnosis and prognosis of AMI patients by analyzing a series of clinical data. The objective was to provide new ideas for the treatment of AMI.

Materials and methods

Study subjects

The AMI group included 90 patients with AMI who were treated at Wenzhou People's Hospital between October 2022 to October 2023. Inclusion criteria: (1) the relevant diagnosis meets the criteria in the Clinical Practice Guideline of Integrative Chinese and Western Medicine for Acute Myocardial Infarction [17]; (2) all of them received echocardiography and coronary arteriography (CAG) examination in our hospital; (3) there is no previous history of AMI. Exclusion criteria: (1) patients with tuberculosis and other pathogenic infections; (2) patients with malignant tumors and other serious diseases; (3) patients with congenital heart disease. The control group consisted of 50 patients who were admitted to the hospital for non-cardiogenic chest pain during the same period. The diagnosis of AMI was excluded based on the patient's presenting symptoms, medical history, laboratory test results, and imaging findings. All patients in the control group also received echocardiography and laboratory index tests, etc. The study was approved by the Ethics Committee of Wenzhou People's Hospital and informed consent was also obtained from the patients and their families.

Basic information such as sex, age, BMI, history of smoking, and history of diabetes or hypertension were recorded for the study population.

Echocardiography

Echocardiography was performed using a Vivid E95 color Doppler ultrasound instrument (General Electric Company, USA), with a probe (frequency of 2–4 MHz). The patient was placed in the lying position, and the chest and heart position were scanned, and the coordination of ventricular wall movement, amplitude of movement, and intensity of echo were targeted for observation and recording of the apical four-chamber and two-chamber views of the parasternal left ventricle in the parasternal left ventricular long- and short-axis views. The assessment of ventricular wall motion abnormalities was conducted through a qualitative analysis of ventricular wall motion in each segment. (1) normal or enhanced motion: endocardial motion of ≥5 mm and ≥50% ventricular wall thickening; (2) diminished motion: endocardial motion of 2 to 4 mm and <50% ventricular wall thickening; (3) the disappearance of motion, which may manifest as the disappearance of ventricular wall thickening or as negligible

ventricular wall thickening, with endocardial motion measuring less than 2 mm; and (4) reverse motion, which presents as thinning or elongation of the myocardium during systole, with ventricular wall motion directed outward. The above myocardial motion was scored as enhanced motion: 0; normal motion: 1; reduced motion: 2; absent motion: 3; and reversed motion: 4. After averaging the scores of all segments, the LV wall motion score index (WMSI) was calculated, with WMSI=1 as normal, > 1 as abnormal, and >2 as significantly abnormal. Moreover, these evaluations were performed blinded at the miR-199a-5p level. The left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and left ventricular ejection fraction (LVEF) were measured and calculated using the Simpson's biplane method.

Follow-up

Patients with AMI were followed up for 6 months to document the occurrence of MACE, which included heart failure, malignant arrhythmia, recurrent AMI, and all-cause death. The diagnostic criteria for heart failure and malignant arrhythmia were referred to Chinese heart failure diagnosis and treatment guidelines 2018 [18] and Chinese expert consensus on ventricular arrhythmia [19], respectively. These events were confirmed by two experienced clinicians based on a comprehensive assessment of the patient's clinical presentation, laboratory test results, and imaging findings. Patients with AMI who developed MACE were categorized in the MACE group, otherwise, they were classified in the non-MACE group.

Table 1 Baseline features of the study subjects

Clinical feature	AMI patients($n=90$)	Control ($n=50$)	P value
Age (years)	60.64 ± 8.77	59.68 ± 8.68	0.532
Sex (male/female)	50/40	27/23	0.859
BMI (kg/m^2)	24.95 ± 4.58	24.30 ± 4.25	0.410
Smoking (no/yes)	51/39	28/22	0.939
Hypertension (no/yes)	38/52	27/23	0.181
Diabetes (no/yes)	50/40	31/19	0.459
TC (mmol/L)	4.77 ± 0.98	4.57 ± 0.92	0.234
TG (mmol/L)	1.75 ± 0.45	1.66 ± 0.33	0.174
HDL-C (mmol/L)	1.16 ± 0.26	1.20 ± 0.29	0.362
LDL-C (mmol/L)	2.79 ± 0.56	2.62 ± 0.51	0.085
CK-MB (ng/mL)	14.13 ± 4.06	2.86 ± 0.80	< 0.001
cTnI (μg/L)	1.82 ± 0.63	0.08 ± 0.04	< 0.001
NT-proBNP (ng/L)	1533.32 ± 351.42	99.26 ± 33.43	< 0.001

Abbreviations AMI, acute myocardial infarction; BMI, body mass index; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; CK-MB, creatine kinase-myocardial bland; cTnI, cardiac troponin I; NT-proBNP, N-terminal pro-B-type natriuretic peptide

Detection of serum miR-199a-5p

Blood collection was performed at the time of admission. The serum was obtained by centrifuging 2 mL of venous blood at 3500 rpm for 10 min. RNA was extracted with RNAiso for Small RNA (TaKaRa, Japan) and then reverse transcribed using PrimeScrip RT Master Mix (TaKaRa). The concentration and purity of RNA was assessed using a NanoDrop microspectrophotometer (Thermo Scientific, USA) with OD260/OD280 ranging from 1.8 to 2.0. cDNA was used as the template to prepare the system according to TB Green Fast qPCR Mix (TaKaRa) instructions and RT-qPCR was performed on CFX96 RT-qPCR system (Bio-Rad, USA). The relative levels of miR-199a-5p were calculated by the $2^{-\Delta\Delta CT}$ method using cel-miR-39 as a reference. The primers were as follows: miR-199a-5p, forward-5'-GCCAAGCCCAGTGTTCAGAC-3', reverse-5'-GTGCAGGGTCCGAGGTATTC-3'; cel-miR-39, forward-5'-GGCGTCACCGGGTAAA-3', reverse-5'-AGTGCAGGGTCCGAGGTATT-3'. The reaction was conducted at 95 °C for 30 s, followed by 95 °C for 5 s and 60 °C for 10 s (40 cycles).

Statistical methods

Statistical analyses were carried out using SPSS 22.0. Measurements were expressed as mean ± SD, and comparisons between groups were made using the t-test. Count data were expressed as cases (n), and comparisons between groups were made using the chi-square test. The correlation of serum miR-199a-5p with LVEF and cTnI was determined by Spearman's method. The value of miR-199a-5p combined with echocardiography in the diagnosis and prognosis of AMI was evaluated by ROC curves, and the prognostic value was further analyzed by Kaplan-Meier curve and Cox regression analysis. Differences were significant at $P<0.05$.

Results

Serum miR-199a-5p levels correlated with LVEF and cTnI levels

The differences in CK-MB, cTnI, and NT-proBNP between AMI patients and controls were statistically significant ($P<0.001$), while other clinical characteristics were not significantly different ($P>0.05$, Table 1). miR-199a-5p was markedly upregulated in AMI patients compared to controls (Fig. 1A). The values of echocardiography parameters LVEDV and LVESV were higher in AMI patients than in the control population, whereas the LVEF values were lower than in the control population ($P<0.001$, Table 2). Moreover, miR-199a-5p expression in AMI patients was positively correlated with cTnI levels ($r=0.607$, $P<0.001$, Fig. 1B) and negatively correlated with LVEF ($r=-0.535$, $P<0.001$, Fig. 1C).

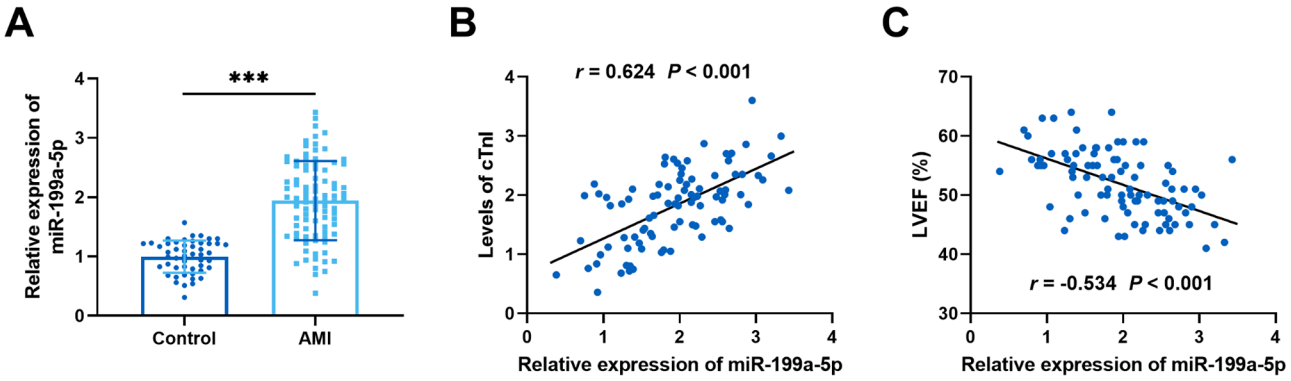

Fig. 1 Association of serum miR-199a-5p with AMI. **A.** miR-199a-5p expression in AMI patients ($n=90$) and control population ($n=50$). **B-C.** Correlation analysis of miR-199a-5p with cTnI (**B**) and LVEF (**C**)

Table 2 Echocardiography parameters of the study subjects

Parameter	AMI patients($n=90$)	Control ($n=50$)	*P* value
LVEDV (mL)	122.36 ± 22.60	96.12 ± 11.59	< 0.001
LVESV (mL)	53.04 ± 5.62	47.02 ± 7.08	< 0.001
LVEF (%)	52.00 ± 5.53	61.12 ± 5.27	< 0.001

Abbreviations AMI, acute myocardial infarction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVEF, left ventricular ejection fraction

Serum miR-199a-5p combined with echocardiography had a high value in the diagnosis of AMI

The ROC curve showed that serum miR-199a-5p could identify AMI patients from chest pain patients with an area under the curve (AUC) of 0.902 ($P<0.001$, Fig. 2A). The AUC values for LVEDV, LVESV, and LVEF to diagnose AMI were 0.866, 0.758, and 0.874, respectively ($P<0.001$, Fig. 2B-D). Further analysis revealed that miR-199a-5p combined with LVEDV, LVESV, and LVEF had a higher efficacy in diagnosing AMI, with an AUC value of 0.991, and the sensitivity and specificity were 96.67% and

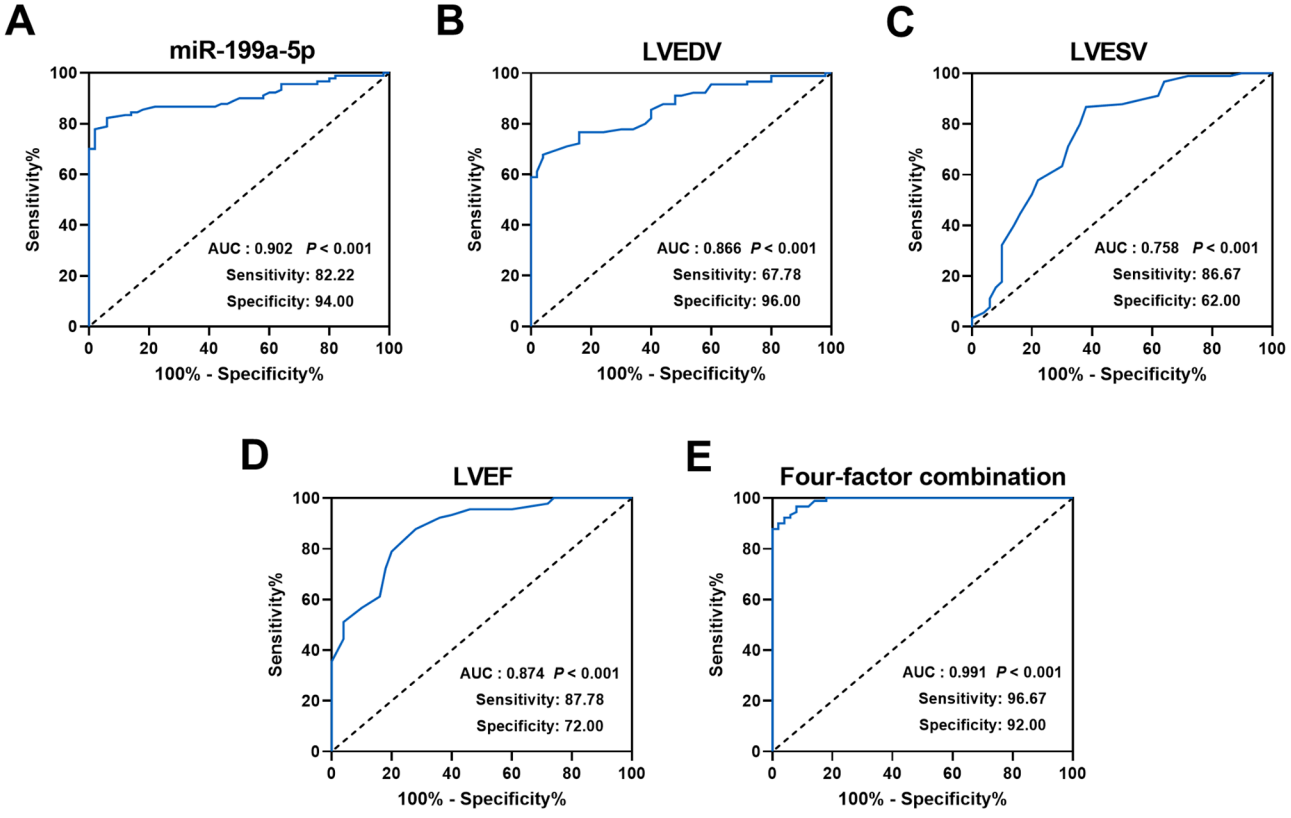

Fig. 2 Diagnostic significance of serum miR-199a-5p in combination with echocardiography. **A-E.** Value of miR-199a-5p (**A**), LVEDV (**B**), LVESV (**C**), LVEF (**D**), and four-factors combination (**E**) in the diagnosis of AMI

Table 3 Clinical features of the MACE and non-MACE groups

Clinical feature	MACE group ($n=25$)	Non-MACE group ($n=65$)	*P* value
Age (years)	62.40 ± 8.50	59.97 ± 8.84	0.241
Sex (male/female)	16/9	34/31	0.317
BMI (kg/m^2)	24.57 ± 3.57	25.10 ± 4.94	0.410
Smoking (no/yes)	12/13	39/26	0.303
Hypertension (no/yes)	10/15	28/37	0.791
Diabetes (no/yes)	11/14	39/26	0.171
TC (mmol/L)	5.02 ± 0.98	4.67 ± 0.97	0.132
TG (mmol/L)	1.78 ± 0.47	1.73 ± 0.44	0.691
HDL-C (mmol/L)	1.09 ± 0.26	1.18 ± 0.25	0.116
LDL-C (mmol/L)	2.92 ± 0.37	2.74 ± 0.61	0.098
CK-MB (ng/mL)	16.02 ± 4.31	13.40 ± 3.75	0.005
cTnI (μg/L)	2.07 ± 0.46	1.73 ± 0.66	0.007
NT-proBNP (ng/L)	1729.00 ± 319.44	1458.06 ± 335.80	0.001
Killip grade (I-II/III-IV)	11/14	45/20	0.027

Abbreviations MACE, major adverse cardiovascular events; BMI, body mass index; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; CK-MB, creatine kinase-myocardial bland; cTnI, cardiac troponin I; NT-proBNP, N-terminal pro-B-type natriuretic peptide

Table 4 Echocardiography parameters of the MACE and non-MACE groups

Parameter	MACE ($n=25$)	Non-MACE ($n=65$)	*P* value
LVEDV (mL)	125.52 ± 18.59	121.14 ± 21.34	0.369
LVESV (mL)	54.80 ± 5.87	52.37 ± 5.41	0.066
LVEF (%)	49.28 ± 4.39	53.05 ± 5.60	0.003

Abbreviations MACE, major adverse cardiovascular events; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVEF, left ventricular ejection fraction

92.00%, respectively ($P<0.001$, Fig. 2E). The optimal cut-off value for miR-199a-5p was 1.310.

Serum miR-199a-5p combined with echocardiography could predict the occurrence of MACE

MACE occurred in 25 patients within 6 months of AMI, including 12 cases of heart failure, 6 cases of malignant arrhythmia, 4 cases of recurrent AMI, and 3 cases of cardiac death. Patients were categorized into MACE ($n=25$) and non-MACE ($n=65$) groups according to whether MACE occurred or not. Patients in the MACE group had remarkably higher levels of CK-MB, cTnI, and NT-proBNP than those in the non-MACE group, and Killip grade also showed a significant difference ($P<0.05$, Table 3). LVEF was markedly lower in the MACE group than in the non-MACE group (Table 4), while serum miR-199a-5p levels were significantly higher (Fig. 3A). Serum miR-199a-5p was associated with the incidence of MACE, and patients with higher miR-199a-5p levels had lower MACE-free survival (Log-rank, $P=0.043$, Fig. 3B). miR-199a-5p, (HR = 2.954, $P=0.028$), LVEF (HR = 0.327, $P=0.040$), cTnI (HR = 3.191, $P=0.038$), and Killip grade (HR = 2.555, $P=0.038$) were independent predictors of MACE (Fig. 3C).

In addition, the AUC values for miR-199a-5p and LVEF predicted MACE were 0.685 and 0.696, respectively ($P<0.01$, Fig. 4A and B). More importantly, miR-199a-5p combined with LVEF predicted MACE with an AUC value of 0.753, and the sensitivity and specificity were 84.00% and 55.38%, respectively ($P<0.001$, Fig. 4C). The optimal cutoff value for miR-199a-5p was 1.975.

Discussion

The clinical manifestations of AMI are chest pain, arrhythmia, acute circulatory dysfunction, and elevated serum levels of markers of cardiac injury. However, the clinical manifestations of AMI are complex and variable, some patients do not have typical chest pain symptoms, and early changes are weaker in patients with smaller infarction areas [20, 21]. More and more studies are exploring new ways to diagnose and assess AMI [22, 23]. miRNAs are useful biomarkers of early pathological and physiological changes in diseases, exhibiting excellent stability and resistance to degradation by RNA enzymes. Previous studies have indicated that miRNAs are closely

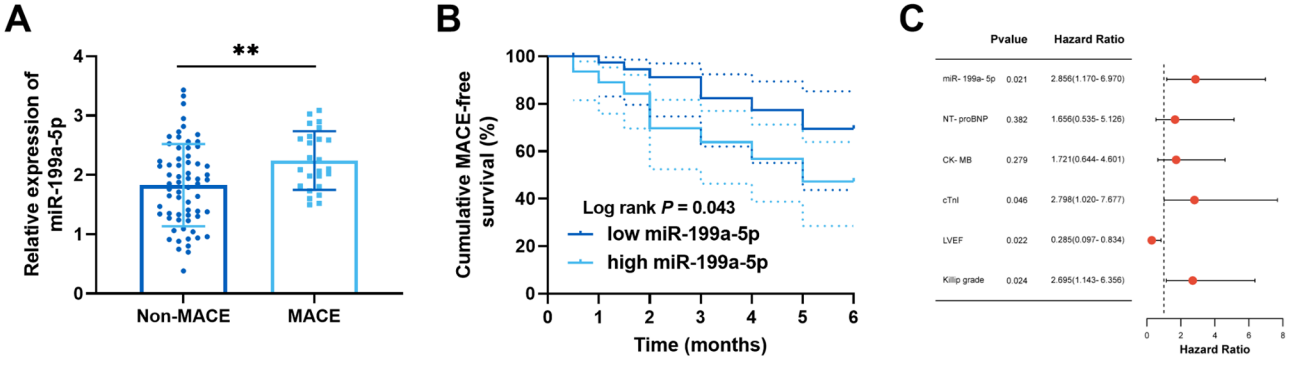

Fig. 3 The relationship between miR-199a-5p and the occurrence of MACE within 6 months. (**A**) miR-199a-5p expression in patients with MACE ($n=25$) and non-MACE ($n=65$). (**B**) Association of miR-199a-5p levels with MACE-free survival of patients. (**C**) Analysis of predictive factors for the development of MACE in patients

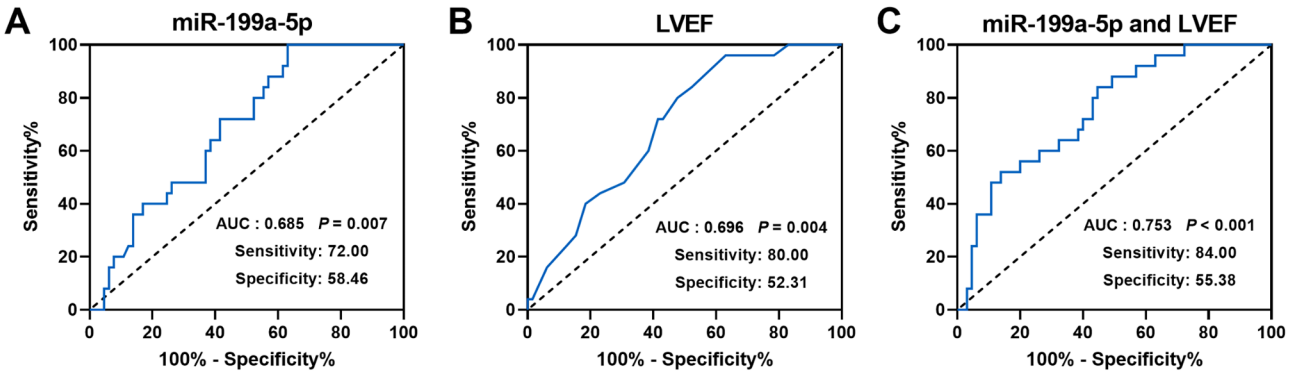

Fig. 4 Prediction of MACE occurrence by serum miR-199a-5p combined with LVEF. **A-C.** Value of miR-199a-5p (**A**), LVEF (**B**), and the combination of them (**C**) for predicting MACE occurrence in patients

associated with cardiac diseases and have the potential to serve as indicators of ventricular remodeling [24, 25]. The current study focused on the diagnostic and prognostic value of serum miR-199a-5p combined with echocardiography in AMI.

In this study, serum miR-199a-5p level in AMI patients was markedly increased, which coincided with previous research [26]. This study also found that LVEDV and LVESV were markedly higher in AMI patients, while LVEF was significantly lower. This suggests that AMI patients have significant abnormalities in the relevant kinetic parameters of myocardial infarcted tissues due to the segmental motion of the ventricular wall in the infarcted area being disturbed, weakened, or even ceased [27]. Additionally, a significant correlation was found between miR-199a-5p with cTnI and LVEF, indicating that miR-199a-5p is closely associated with myocardial injury as well as altered cardiac function in AMI patients. miR-199a-5p was also reported to be upregulated in the AMI rat model and increased with the progression of heart failure [28, 29]. Therefore, the detection of miR-199a-5p has great potential to assess the extent of myocardial infarction in patients.

Some miRNAs are considered potential biomarkers for AMI and may be useful for early diagnosis of AMI [30]. For example, it was found that the combination of miR-145-3p, miR-126-5p, and miR-17-5p was able to provide a more accurate diagnosis of AMI [31]. Another research also found that the combined use of plasma miR-203 and miR-4516 may potentially serve as a diagnostic and severity assessment tool for AMI [32]. This study demonstrated the high value of miR-199a-5p in differentiating AMI patients from the control population. Moreover, the combined use of serum miR-199a-5p, LVEDV, LVESV, and LVEF was more effective than the use of individual indicators in the diagnosis of AMI. This suggests that the combination of miR-199a-5p and echocardiographic parameters could somewhat compensate for the inadequacy of a single index.

LVEF is an important echocardiographic parameter that reflects reduced systolic function due to persistent myocardial ischemia or injury. LVEF was demonstrated to be a significant predictor of short-term outcomes in patients with AMI [33, 34]. Here, further analysis revealed that miR-199a-5p in combination with LVEF improved the predictive value of developing MACE in AMI patients. Previously, Asensio-Lopez et al. found that pathological cardiac hypertrophy and fibrosis could be attenuated by inhibiting miR-199a-5p expression in mice with myocardial infarction [28]. Moreover, Liu et al. demonstrated that plasma miR-199a-5p levels were elevated in AMI patients and that upregulation of miR-199a-5p in vitro resulted in I/R injury in cardiomyocytes [26]. These findings support the results of the clinical analyses in our study. The current study also showed that AMI patients with higher levels of miR-199a-5p had reduced MACE-free survival. In addition, miR-199a-5p and LVEF showed significant prognostic potential. Therefore, miR-199a-5p combined with echocardiography could be used as a prognostic reference for AMI patients, which may help to adopt a more effective and targeted therapeutic regimen in clinical management.

However, the single and small source of clinical data leads to the need for further validation of the results. Furthermore, the molecular mechanisms of miR-199a-5p in the pathological process of AMI require further investigation. In particular, subsequent studies will focus on the role of miR-199a-5p-regulated target genes in the progression of AMI and delve into the regulatory mechanisms involved in miR-199a-5p. In summary, serum miR-199a-5p levels were increased in AMI patients, and miR-199a-5p combined with echocardiography parameters had a better prospect for differential diagnosis of AMI and prediction of MACE.

Acknowledgements
Not applicable.

Author contributions
Conceptualization, L.X. and J.L.; Data curation, J.X., D.C. and G.H.; Formal analysis, D.C. and G.H.; Funding acquisition, J.L.; Investigation, J.X., D.C. and G.H.; Methodology, J.X., D.C. and G.H.; Project administration, J.L.; Resources, J.X.,

D.C. and G.H.; Software L.X.; Supervision, J.L.; Validation, L.X., J.X., D.C. and G.H.; Visualization, J.L.; Roles/Writing - original draft, L.X.; Writing - review & editing, J.L.

Funding
No funding was received to assist with the preparation of this work.

Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Wenzhou People's Hospital (Date: 15 March 2022/No. 2022-031).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 13 August 2024 / Accepted: 24 December 2024
Published online: 07 January 2025

References

1. Boateng S, Sanborn T. Acute myocardial infarction. Dis Mon. 2013;59(3):83–96.
2. Pasupathy S, La S, Tavella R, Zeitz C, Worthley M, Sinhal A, et al. Do chest pain characteristics in patients with acute myocardial infarction differ between those with and without obstructive coronary artery disease? J Clin Med. 2023;12(14):4595.
3. Zhang P, Wu L, Zou TT, Zou Z, Tu J, Gong R, et al. Machine learning for early prediction of major adverse cardiovascular events after first percutaneous coronary intervention in patients with acute myocardial infarction: Retrospective Cohort Study. JMIR Form Res. 2024;8(1):e48487.
4. Al-Zaiti SS, Martin-Gill C, Zegre-Hemsey JK, Bouzid Z, Faramand Z, Alrawashdeh MO, et al. Machine learning for ECG diagnosis and risk stratification of occlusion myocardial infarction. Nat Med. 2023;29(7):1804–13.
5. Wang XY, Zhang F, Zhang C, Zheng LR, Yang J. The biomarkers for acute myocardial infarction and heart failure. Biomed Res Int. 2020;2020(1):2018035.
6. Boeddinghaus J, Reichlin T, Nestelberger T, Twerenbold R, Meili Y, Wildi K, et al. Early diagnosis of acute myocardial infarction in patients with mild elevations of cardiac troponin. Clin Res Cardiol. 2017;106(6):457–67.
7. Chaulin AM. Elevation mechanisms and diagnostic consideration of cardiac troponins under conditions not associated with myocardial infarction. Part 1. Life (Basel). 2021;11(9):914.
8. Guta AC, Badano LP, Ochoa-Jimenez RC, Genovese D, Previtero M, Civera S, et al. Three-dimensional echocardiography to assess left ventricular geometry and function. Expert Rev Cardiovasc Ther. 2019;17(11):801–15.
9. El-Naggar HM, Osman AS, Ahmed MA, Youssef AA, Ahmed TAN. Three-dimensional echocardiographic assessment of left ventricular geometric changes following acute myocardial infarction. Int J Cardiovasc Imaging. 2023;39(3):607–20.
10. Zhang Y, Zhao Z, Zheng L, Zhang T, Sun X. Three-dimensional echocardiography and coagulation function detection in the prognosis evaluation of patients with acute myocardial infarction. Comput Math Methods Med. 2022;2022(1):5197871.
11. Su J, Li J, Yu Q, Wang J, Li X, Yang J, et al. Exosomal miRNAs as potential biomarkers for acute myocardial infarction. IUBMB Life. 2020;72(3):384–400.
12. Wang Y, Chang W, Zhang Y, Zhang L, Ding H, Qi H, et al. Circulating mir-22-5p and mir-122-5p are promising novel biomarkers for diagnosis of acute myocardial infarction. J Cell Physiol. 2019;234(4):4778–86.
13. Ren L, Liu W, Chen S, Zeng H. Longitudinal change of serum exosomal mir-186-5p estimates major adverse cardiac events in acute myocardial infarction patients receiving percutaneous coronary intervention. Front Cardiovasc Med. 2024;11:1341918.
14. Qiao S, Wang X, Li H, Zhang C, Wang A, Zhang S. Atherosclerosis-associated endothelial dysfunction is promoted by miR-199a-5p/SIRT1 axis regulated by circHIF1a. Nutr Metab Cardiovasc Dis. 2023;33(8):1619–31.
15. Tian X, Yu C, Shi L, Li D, Chen X, Xia D, et al. MicroRNA-199a-5p aggravates primary hypertension by damaging vascular endothelial cells through inhibition of autophagy and promotion of apoptosis. Exp Ther Med. 2018;16(2):595–602.
16. Zhang GY, Gao Y, Guo XY, Wang GH, Guo CX. MiR-199a-5p promotes ferroptosis-induced cardiomyocyte death responding to oxygen-glucose deprivation/reperfusion injury via inhibiting Akt/eNOS signaling pathway. Kaohsiung J Med Sci. 2022;38(11):1093–102.
17. Liao PD, Chen KJ, Ge JB, Zhang MZ. Clinical Practice Guideline of Integrative C Western Medicine for Acute Myocardial Infarction Working G. Clinical Practice Guideline of Integrative Chinese and Western Medicine for Acute myocardial infarction. Chin J Integr Med. 2020;26(7):539–51.
18. Association CBoCM. Chinese heart failure diagnosis and treatment guidelines 2018. Chin J Cardiovasc Dis. 2018;46(10):760.
19. Cao K, Chen K, Chen M, Hong K, Hua W, Huang C. Chinese expert consensus on ventricular arrhythmia. Chin J Card Pac Electrophysiol. 2016;30(4):283–325.
20. Zeymer U. [Diagnosis and initial management of acute myocardial infarction]. MMW Fortschr Med. 2019;161(4):34–6.
21. Leite WF, Dos Santos Povoa RM, Caixeta AM, Amodeo C, Szarf G, Bombig MTN, et al. Chest Pain in Acute Myocardial Infarction and its Association with the Culprit Artery and Fibrotic Segment identified by Cardiac magnetic resonance. Cardiol Res. 2023;14(2):97–105.
22. Zhang N, Zhou B, Tu S. Identification of an 11 immune-related gene signature as the novel biomarker for acute myocardial infarction diagnosis. Genes Immun. 2022;23(7):209–17.
23. Huang Y, Li Y, Zhang K, Xu J, Li P, Yan X, et al. Expression and diagnostic value of PIWI-interacting RNA by serum in acute myocardial infarction. J Cardiol. 2023;82(6):441–7.
24. Colpaert RMW, Calore M. MicroRNAs in Cardiac Diseases. Cells. 2019;8(7):737.
25. Pang JKS, Phua QH, Soh BS. Applications of miRNAs in cardiac development, disease progression and regeneration. Stem Cell Res Ther. 2019;10(1):336.
26. Liu DW, Zhang YN, Hu HJ, Zhang PQ, Cui W. Downregulation of microRNA–199a–5p attenuates hypoxia/reoxygenation–induced cytotoxicity in cardiomyocytes by targeting the HIF–1alpha–GSK3beta–mPTP axis. Mol Med Rep. 2019;19(6):5335–44.
27. De Giorgio D, Olivari D, Fumagalli F, Staszewsky L, Ristagno G. Transthoracic echocardiography to assess post-resuscitation left ventricular dysfunction after acute myocardial infarction and cardiac arrest in Pigs. J Vis Exp. 2022;(185):e63888.
28. Asensio-Lopez MC, Sassi Y, Soler F, Fernandez Del Palacio MJ, Pascual-Figal D, Lax A. The miRNA199a/SIRT1/P300/Yy1/sST2 signaling axis regulates adverse cardiac remodeling following MI. Sci Rep. 2021;11(1):3915.
29. Yan M, Yang S, Meng F, Zhao Z, Tian Z, Yang P. MicroRNA 199a-5p induces apoptosis by targeting JunB. Sci Rep. 2018;8(1):6699.
30. Sharma AK, Bisht P, Gupta B, Sayeed Akhtar MD, Shaik Alavudeen S, Afzal O, et al. Investigating miRNA subfamilies: can they assist in the early diagnosis of acute myocardial infarction? Drug Discov Today. 2023;28(10):103695.
31. Xue S, Liu D, Zhu W, Su Z, Zhang L, Zhou C, et al. Circulating MiR-17-5p, MiR-126-5p and MiR-145-3p are novel biomarkers for diagnosis of Acute myocardial infarction. Front Physiol. 2019;10:123.
32. Liu P, Wang S, Li K, Yang Y, Man Y, Du F, et al. Exosomal microRNA–4516, microRNA–203 and SFRP1 are potential biomarkers of acute myocardial infarction. Mol Med Rep. 2023;27(6):1–12.
33. Baron T, Flachskampf FA, Johansson K, Hedin EM, Christersson C. Usefulness of traditional echocardiographic parameters in assessment of left ventricular function in patients with normal ejection fraction early after acute myocardial infarction: results from a large consecutive cohort. Eur Heart J Cardiovasc Imaging. 2016;17(4):413–20.
34. Han MM, Zhao WS, Wang X, He S, Xu XR, Dang CJ, et al. Echocardiographic parameters predict short- and long-term adverse cardiovascular events in patients with Acute myocardial infarction. Int J Gen Med. 2021;14:2297–303.

Publisher's note