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Expressions of miR-132, miR-145 and miR-208 in Patients with Acute Myocardial Infarction and Correlations with Gensini Score

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KEYWORDS Acute Myocardial Infarction. Gensini Score. miRNA

ABSTRACT The researchers aimed to investigate the correlations of miR-132, miR-145 and miR-208 with the Gensini score (GS) of patients with acute myocardial infarction (AMI). Totally 120 AMI patients and 80 healthy volunteers undergoing physical examination were included into AMI group and healthy group, respectively. The AMI patients were subdivided into low GS (LGS) group (≤ 30 points) and high GS (HGS) group (>30 points). Independent risk factors included troponin I (TnI), creatine kinase (CK) isoenzyme, uric acid (UA), C-reactive protein (CRP), miR-132, miR-145 and miR-208, which affected the severity of coronary artery lesions (CALs) ($P<0.05$). Compared with miR-132, miR-145, and miR-208 alone, their combination had the highest diagnostic value, with the area under curve (95%CI) of 0.911 (0.869-0.978), sensitivity of 89.89 percent and specificity of 70.91 percent ($P<0.001$). MiR-132, miR-145, and miR-208 are abnormally expressed in AMI patients. Their combination has higher diagnostic value for the severity of CALs in AMI patients.

INTRODUCTION

Acute myocardial infarction (AMI), refers to a condition resulting from coronary atherosclerosis, with high incidence and death rates (De-Filippis et al. 2019). The onset of AMI involves endothelial dysfunction as well as instability and rupture of atherosclerotic plaques induced by many factors (Ueda et al. 2021; El-Shetry et al. 2021). With rapid onset and progression, this disease threatens the life of patients, so the early assessment of the severity of coronary artery lesions (CALs) in AMI patients is of great significance for developing treatment regimens and improving the prognosis (Gulati et al. 2020). To this end, researchers have endeavoured to find eligible biomarkers (Chen et al. 2019).

Micro ribonucleic acids (miRNAs), as a class of RNAs with approximately 22 nt in length, are widely distributed in the tissues of the kidney, liver, lung and other organs (Blanco-Domínguez et al. 2021). Their expression levels change dynamically under pathological conditions, which is an accurate reflection of the function and state of cells (Boon and Dimmeler 2015). According to reports, miRNAs are implicated in the onset and progression of malignant tumours, kidney diseases and cardiovascular diseases (CVDs) (Bazzell et al. 2018; Pan et al. 2021). Therefore, miRNAs have been widely applied in the diagnosis of various clinical diseases (Dwivedi et al. 2019). For AMI, miRNAs exhibit higher specificity than that of traditional diagnostic markers (Nouraee and Mowla 2015; Miki and Imamura 2020).

MiR-132, miR-145, and miR-208 belong to the miRNA family. As reported by Su et al. (2020), miR-132 was a mediator for myocardial injury, and its low expression facilitated disease progression. Besides, Hu et al. (2018) uncovered that miR-145 prevented cardiomyocytes from I/R injury, as a mediator under the promoting effect of FGF21. Moreover, as uncovered by Li et al. (2019), the serum miR-208 level in AMI patients dramatically rose relative to those in healthy subjects, so the severity of AMI in patients can be assessed based on the miR-208 expression level. On the other hand, the Gensini score (GS) is a tool for the assessment of the severity of CALs, which is calculated by summation of the scores assigned for coronary artery stenosis and lesion site (Rampidis et al. 2019). The association of other miRNAs with the severity of AMI has been explored based on this score (Guo et al. 2018). However, the correlations of miR-132, miR-145 and miR-208 with the GS of AMI patients have never been reported.

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Objectives

In this study, the combination of miR-132, miR-145 and miR-208 was adopted for determining the severity of CALs in AMI patients, and the correlations of the three indicators with GS were analysed, aiming to provide potentially applicable biomarkers for AMI prevention and treatment.

MATERIAL AND METHODS

Clinical Data

This study included totally 120 AMI patients undergoing treatment (AMI group) and 80 healthy volunteers receiving physical examination (healthy group) in the hospital between January 2021 and January 2022. The male/female ratio was 17:13 and 19:21, and the mean age was (56.87±6.91) years old and (56.99±6.64) years old in AMI group and healthy group, respectively. The two groups had comparable basic clinical data (P>0.05).

The inclusion criteria for AMI group were as follows:

1. Patients with ischemic chest pain ≥ 0.5 h;
2. Those with an elevation in the ST segment in ECG leads;
3. Those whose serum cardiac markers [troponin I (TnI) and creatine kinase (CK) isoenzyme]; increased to twice that of the normal value;
4. Those with the onset time ≤ 12 h.

The patients meeting two of the criteria (1), (2) and (3) were diagnosed as AMI. The volunteers without history of cardiovascular disease and in good physical condition were included in healthy group.

The exclusion criteria were set below:

1. Patients with history of myocardial infarction;
2. Those with congenital heart disease;
3. Those with autoimmune diseases;
4. Those undergoing a major surgery recently;
5. Those with malignant tumours;
6. Those with mental disorders;
7. Those with barriers to communication.

Detection of miR-132, miR-145 and miR-208 Expressions

In the morning, 2 mL fasting venous blood was extracted, and mononuclear cells were isolated from the peripheral blood. The expressions of miR-132, miR-145 and miR-208 were examined *via* real-time quantitative polymerase chain reaction (PCR), and the TRIzol method was employed for RNA extraction. Afterwards, the RNAs underwent reverse transcription (RT) into cDNAs by use of a RT kit (TaKaRa, Japan). PCR was conducted using primer sequences designed by Primer 5.0 software on a reaction system (20 μL) consisting of forward primers and reverse primers (0.4 μL each) + 1 μL of cDNA template + 10 μL of SYBR Green + 8.2 μL of distilled water under the following PCR conditions: 5-min pre-denaturation at 95°C + 38 cycles* (30-s denaturation at 94°C, 45-s annealing at 54°C, and 30-s extension at 72°C) + 5-min extension at 72°C. The primers used for PCR included miR-132: F: 5'-GGAGACATGAGAGCTGCCAAC-3', and R: 5'-CCAGCAGCATGTCGAAGATC-3', miR-145: F: 5'-ATCGTCCAGTTTTCCCAGG-3' and R: 5'-CGCCTCCACACACTCACC-3', and miR-208: F: 5'-TGCGGTATAAGACGAGCAAA-3' and R: 5'-ATTCCATGTTGTCCACAGTCTCC-3'. β-Actin gene was taken as internal reference, with F: 5'-GCGAGAAGATGACCCACCACC-3' and R: 5'-ATGTCACGCACGATTTCCTATTA-3'. The $2^{-\Delta\Delta Ct}$ method was employed for the calculation of miR-132, miR-145 and miR-208 expression levels. The detection was carried out three times for each group, and the results were averaged.

Evaluation Criteria for GS

The score for stenosis severity was classified into the following six grades, wherein 1 point was assigned to the stenosis degree <25 percent, 2 points to 25-50 percent, 4 points to 51-75 percent, 8 points to 76-90 percent, 16 points to 91-99 percent, and 32 points to 100 percent. The lesion site score = lesion score × coefficient (left trunk: 5, opening of circumflex branch: 3.5, middle anterior descending branch: 1.5, aorta and first diagonal branch: 1, distal circumflex branch: 1.0, left branch: 0.5, and other branches: 1.0). The GSd ≤ 30, 31-60 and >60 points suggested mild, moderate, and severe CALs, respectively. As per the GS, AMI group was subdivided into low GS group (LGS) (GS ≤ 30 points) and high GS group (HGS) (GS>30 points).

Observation Indicators

The observation indicators were:

1. miR-132, miR-145 and miR-208 expression levels in AMI and healthy groups were compared.

2. The basic clinical data of HGS and LGS groups, including gender, age, body mass index, smoking history, drinking history, complications (diabetes mellitus, hypertension, and hyperlipidaemia), myocardial infarction site, cardiac function grade, number of CALs, and the levels of TnI, CK isoenzyme, uric acid (UA), blood lipid, blood glucose and C-reactive protein (CRP), were analysed. The expression levels of miR-132, miR-145 and miR-208 in the two groups were compared.
3. Logistic regression analysis (LRA) was employed for assessing the influencing factors for the severity of CALs in AMI patients were assessed using.
4. The correlations of miR-132, miR-145 and miR-208 with the GS were analysed.
5. The values of miR-132, miR-145 and miR-208 in the diagnosis of the severity of CALs in AMI patients were assessed by receiver operating characteristic (ROC) curves.

Statistical Analysis

SPSS 22.0 software was adopted for data processing. The Kolmogorov-Smirnov test was implemented to determine whether data are normally distributed. The measurement data in keeping with normal distribution were described as mean ± standard deviation ($\bar{x} \pm s$). The homogeneity test of variance and independent samples *t*-test were employed for intergroup and intragroup comparisons of measurement data, respectively. Count data were described as frequency and percentage, and intergroup comparison was carried out by the χ^2 test. The influencing factors for the severity of CALs in AMI patients were assessed by LRA, and the correlations of miR-132, miR-145 and miR-208 with the GS were explored by Pearson's analysis. The values of miR-132, miR-145 and miR-208 in the diagnosis of the severity of CALs in AMI patients were analysed by use of ROC curves. P<0.05 was deemed as statistical significance.

RESULTS

Expressions of miR-132, miR-145 and miR-208 in AMI and Healthy Groups

As illustrated in Table 1, the AMI group had lower miR-132 and miR-145 expression levels but a higher miR-208 expression level than healthy group (P<0.05).

Table 1: Expressions of miR-132, miR-145 and miR-208 in AMI and healthy groups ($\bar{x} \pm s$)

	AMI group (n=120)	*Healthy group (n= 80)*	*t*	*P*
miR-132	0.78±0.06	2.23±0.96	16.520	<0.001
miR-145	0.67±0.05	1.87±0.32	40.400	<0.001
miR-208	1.59±0.21	0.20±0.03	58.760	<0.001

AMI: Acute myocardial infarction

Basic Clinical Data and miR-132, miR-145 and miR-208 Expressions in HGS and LGS Groups

The gender ratio, age, BMI, smoking history, drinking history, complications, myocardial infarction site, cardiac function grade, blood lipid, blood glucose and other basic clinical data were not significantly different between HGS and LGS groups (P>0.05). However, HGS group had higher levels of TnI, CK isoenzyme, UA and CRP, a higher miR-208 expression, a higher GS, and lower expressions of miR-132 and miR-145 than LGS group (P<0.05) (Table 2).

Influencing Factors for Severity of CALs in AMI Patients Determined by LRA

LRA was performed with the severity of CALs in AMI patients as a dependent variable (GS ≤ 30 points=0, GS>30 points=1), and TnI, CK isoenzyme, UA, CRP, miR-132, miR-145 and miR-208 displaying significant differences as independent variables (Table 2). As unveiled in Table 3, it appeared that independent risk factors included TnI, CK isoenzyme, UA, CRP, miR-132, miR-145 and miR-208, which influenced the severity of CALs in AMI patients (P<0.05) (Table 3).

Analysis Results of Correlations of miR-132, miR-145 and miR-208 with GS

As unveiled by Pearson's analysis, negative correlations were detected between miR-132 and GS (r=-0.576, P<0.001) and between miR-145 and GS (r=-0.544, P<0.001), and a positive association was observed between miR-208 and GS (r=0.511, P<0.001) (Fig. 1).

Table 2: Basic data and miR-132, miR-145 and miR-208 expressions in HGS and LGS groups

		Low Gensini score group (n=78)	*High Gensini score group (n=42)*	*t/χ^2*	*P*
Gender	Male	46 (58.97)	22 (52.38)	0.483	0.487
	Female	32 (41.03)	20 (47.62)		
Age (year)	56.81±8.92	56.92± 8.77	0.065	0.948	
BMI (kg/m^2)	23.73±2.37	23.68± 2.39	0.110	0.913	
Smoking history	17 (21.79)	11 (26.19)	0.295	0.587	
Drinking history	12 (15.38)	8 (19.05)	0.264	0.608	
Complication	Diabetes mellitus	18 (23.08)	12 (28.57)	0.440	0.507
	Hypertension	16 (20.51)	7 (16.67)	0.261	0.610
	Hyperlipoidemia	10 (12.82)	5 (11.90)	0.021	0.885
Myocardial infarction site	Anteroseptal wall	31 (39.74)	15 (35.71)	0.712	0.870
	Extensive anterior wall	28 (35.90)	15 (35.71)		
	Inferior wall	14 (17.95)	10 (23.81)		
	Other sites	5 (6.41)	2 (4.76)		
Cardiac function grade	Grade I	18 (23.08)	10 (23.81)	0.008	0.928
	Grade II-III	60 (76.92)	32 (76.19)		
Troponin I (μg/L)	1.36±0.11	1.89± 0.23	17.080	<0.001	
Creatine kinase isoenzyme (U/L)	32.41±4.55	40.91± 6.81	8.160	<0.001	
Uric acid (μmol/L)	356.92±57.81	412.31± 90.82	4.074	<0.001	
Blood lipid	Total cholesterol (mmol/L)	4.12± 0.23	4.18±0.33	1.165	0.246
	Triglyceride (mmol/L)	1.58± 0.19	1.63±0.20	1.350	0.180
	High-density lipoprotein cholesterol (mmol/L)	1.32± 0.10	1.35±0.16	1.262	0.209
	Low-density lipoprotein cholesterol (mmol/L)	2.45± 0.21	2.47±0.28	0.442	0.660
Blood glucose	Glycosylated hemoglobin (%)	6.08± 0.20	6.12±0.19	1.063	0.290
	Fasting blood glucose (mmol/L)	4.12± 0.22	4.17±0.23	1.169	0.245
C-reactive protein (mg/L)	4.11±0.26	6.87± 0.96	23.890	<0.001	
MiR-132	1.02±0.11	0.50± 0.08	27.010	<0.001	
MiR-145	0.98±0.08	0.45± 0.04	40.260	<0.001	
MiR-208	1.02±0.20	2.21± 0.34	24.150	<0.001	
Gensini score (point)	23.89±3.91	59.08± 10.33	26.800	<0.001	

AMI: Acute myocardial infarction; BMI: body mass index

Table 3: LRA of factors influencing the severity of CALs in AMI patients

	β	*SE*	*Wald value*	*P*	*OR value*	*95% confidence interval (95% CI)*
Constant	-11.982	5.762	6.892	0.000	-	-
Troponin ±	3.672	0.671	11.082	0.007	1.801	1.042~2.351
Creatine kinase isoenzyme	2.716	0.589	15.990	<0.001	2.976	2.514~3.556
Uric acid	2.833	0.713	13.483	<0.001	2.029	1.786~3.011
C-reactive protein	3.231	0.615	9.002	0.005	1.828	1.009~2.361
MiR-132	2.456	0.781	28.765	<0.001	3.631	2.314~4.082
MiR-145	3.720	0.629	31.990	<0.001	2.976	2.003~3.365
MiR-208	3.891	0.681	33.483	<0.001	3.029	2.078~3.807

AMI: Acute myocardial infarction

Diagnostic Values of miR-132, miR-145 and miR-208 for the Severity of CALs in AMI Patients

The ROC curves revealed that compared with miR-132, miR-145 and miR-208 alone, their combination had the highest diagnostic value for the degree of CALs in AMI patients, with an area under the curve (95%CI) of 0.911 (0.869-0.978), sensitivity of 89.89 percent and specificity of 70.91 percent (P<0.001) (Table 4 and Fig. 2).

DISCUSSION

MiR-132 is located in the intergenic region on the chromosome 17p13.3, and its expression is regulated by elements for adenylate cyclase reaction (Salemi et al. 2018). In addition, miR-132 shows tissue specificity and exerts vital effects on immune system diseases, neurodegenerative diseases, malignant tumours and atherosclerosis (Wang et al. 2020). Up to date, miR-132 exhibits its wide involvement in the onset and progression of AMI, which resists myocardial cell apo-

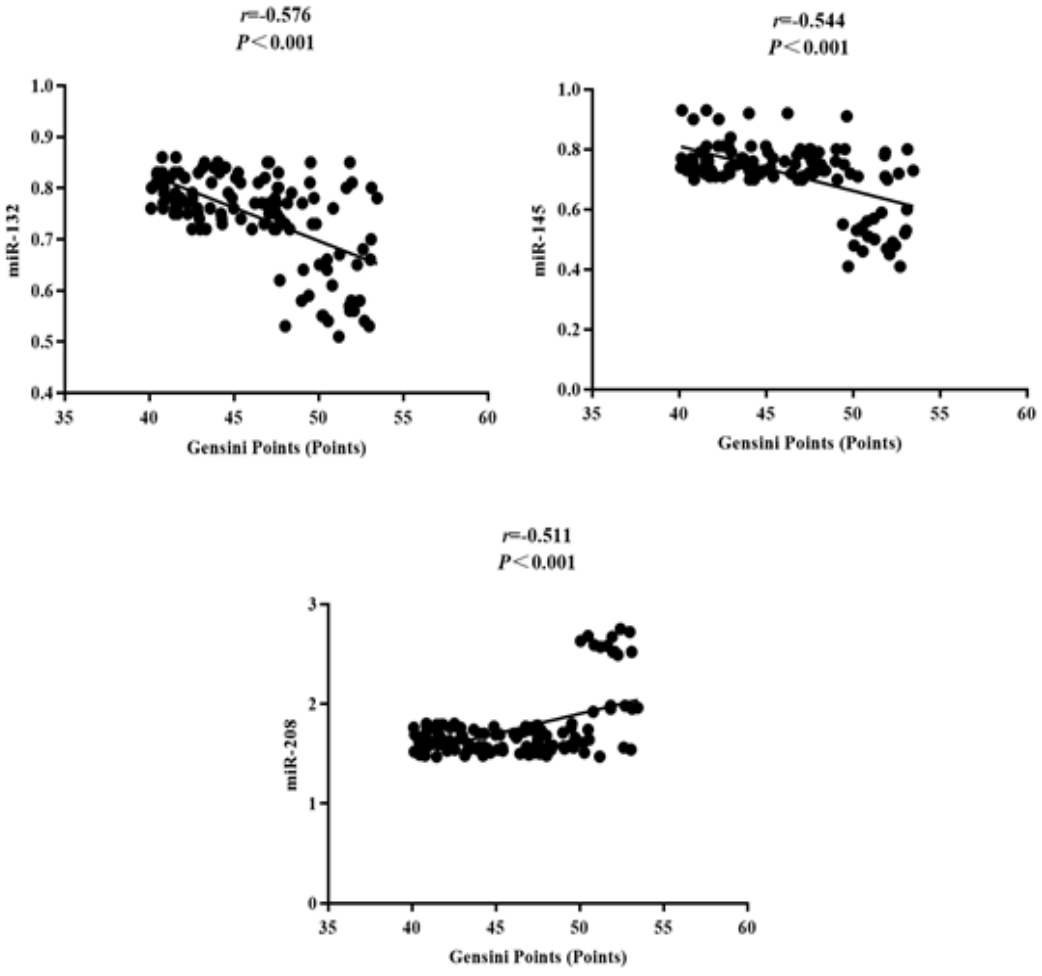

Fig. 1. Correlations of miR-132, miR-145 and miR-208 with GS

Table 4: Efficiencies of miR-132, miR-145 and miR-208 for diagnosis of the severity of CALs in AMI patients

	Area under curve (95%CI)	*Sensitivity (%)*	*Specificity (%)*	*P*	*Cut-off value*
miR-132	0.851 (0.701~0.884)	84.53	73.19	0.001	0.89
miR-145	0.762 (0.592~0.879)	82.11	75.76	0.014	0.67
miR-208	0.760 (0.589~0.855)	82.02	76.85	0.015	1.76
Combination	0.911 (0.869~0.978)	89.89	70.91	<0.001	-

AMI: Acute myocardial infarction

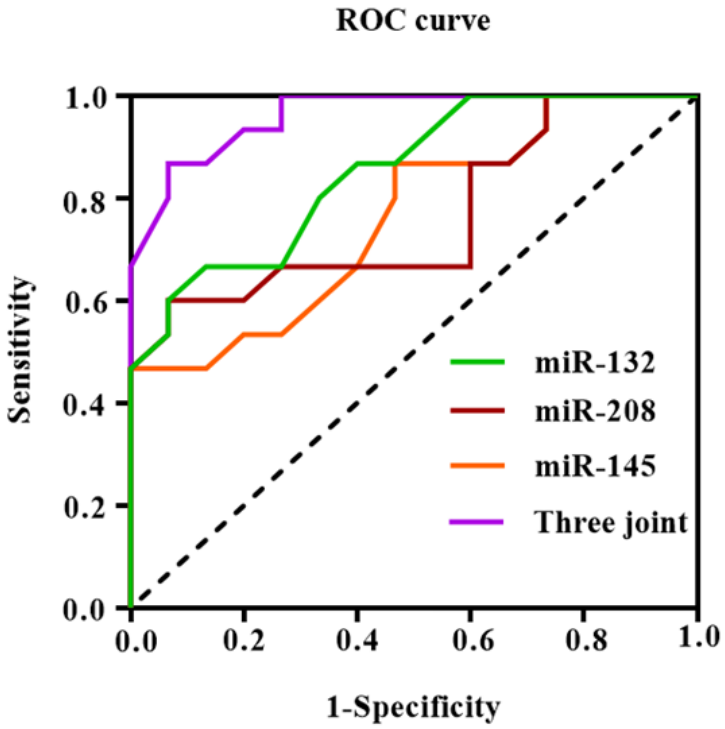

Fig. 2. ROC curves of miR-132, miR-145 and miR-208 for diagnosing the severity of CALs in AMI patients. AMI: Acute myocardial infarction; ROC: receiver operating characteristic

ptosis and alleviates the damage of oxidative stress to myocardial cells (Lei et al. 2021; Liu et al. 2022). Likewise, animal experiments showed that miR-132 relieved ventricular remodelling and myocardial cell apoptosis after MI (Chen et al. 2019; Zhao et al. 2020). In this study, an evident decline was detected in the miR-132 expression in AMI group relative to that in healthy group, and this decrease showed a positive linear relationship with the GS. The results further verified the role of miR-132 in AMI, being consistent with previous literature.

MiR-145 primarily participates in pathological processes such as cardiomyocyte apoptosis, myocardial hypertrophy, ventricular remodelling, heart failure and arrhythmia. It is lowly expressed in cardiomyocytes when the high-glucose state lasts for a long time (Xu et al. 2017; Sun et al. 2018). Higashi et al. (2015) reported that miR-145 targeted fibroblast growth factor receptor substrate 2 to induce cardiomyocyte autophagy, thus protecting the heart, reducing the MI area and finally

alleviating AMI symptoms. In this study, miR-145 was lowly expressed in AMI patients, especially in the AMI patients with a high GS. Probably, during AMI, the mitigative effect of miR-145 on myocardial injury was suppressed, and low-level miR-145 failed to repair the CALs along with the course of AMI, thus aggravating the disease. The findings of this study are identical to those of Zhang et al. (2017) that miR-145 expression was low in AMI patients.

The miR-208 expression level directly reflects the degree of myocardial injury such as myocardial hypertrophy and collagen accumulation, so it is a well-accepted sensitive indicator for the evaluation of myocardial injury in AMI patients (Yan et al. 2016; Pinchi et al. 2019; Wang et al. 2021). Widely existing in the intron of heavy chain myosin genes, miR-208 can regulate the expressions of contractile proteins to speed up cardiomyocyte apoptosis (Liu et al. 2015). Herein, an up-regulated expression of miR-208 in AMI patients and a positive correlation between miR-208 expression and GS were unveiled. Taken together, miR-208 may participate in the aggravation of CALs in AMI patients, but the specific action mechanism needs further studies.

GS is an evaluation tool for the severity of CALs in AMI patients (Qin et al. 2019). In this study, therefore, the values of miR-132, miR-145 and miR-208 in diagnosing the severity of CALs in AMI patients were analysed *via* ROC curves, using GS as the starting point. The cut-off values of the three indicators were 0.89, 0.67 and 1.76, respectively, verifying their predictive values for the severity of CALs in the early stage.

CONCLUSION

In summary, AMI patients, especially those with a high GS, have up-regulated expressions of miR-132 and miR-145 and a down-regulated expression of miR-208. The combination of miR-132, miR-145 and miR-208 shows high predictive value for the severity of CALs in AMI patients, so the progression of AMI can be assessed early according to the expression changes of the three indicators. The findings contribute to the formulation of effective treatment and intervention regiments for the early AMI.

RECOMMENDATIONS

Multi-centre studies with a larger sample size should be further performed to validate the results of this study. Besides, the interactions among miR-132, miR-145 and miR-208 in the case of AMI should be analysed.

ABBREVIATIONS

- AMI: Acute myocardial infarction
- BMI: body mass index
- miRNA: micro ribonucleic acid
- PCR: polymerase chain reaction
- ROC: receiver operating characteristic

REFERENCES

Bazzell BG, Rainey WE, Auchus RJ et al. 2018. Human urinary mRNA as a biomarker of cardiovascular disease: A proof-of-principle study of sodium loading in prehypertension. *Circ Genom Precis Med,* 11: e002213.

Blanco-Domínguez R, Sánchez-Díaz R, de la Fuente H et al. 2021. A novel circulating microRNA for the detection of acute myocarditis. *N Engl J Med,* 384: 2014-2027.

Boon RA, Dimmeler S 2015. MicroRNAs in myocardial infarction. *Nat Rev Cardiol,* 12: 135-142.

Chen L, Wang GY, Dong JH et al. 2019. MicroRNA-132 improves myocardial remodeling after myocardial infarction. *Eur Rev Med Pharmacol Sci*, 23: 6299-6306.

Chen Y, Tao Y, Zhang L et al. 2019. Diagnostic and prognostic value of biomarkers in acute myocardial infarction. *Postgrad Med J,* 95: 210-216.

DeFilippis AP, Chapman AR, Mills NL et al. 2019. Assessment and treatment of patients with type 2 myocardial infarction and acute nonischemic myocardial injury. *Circulation,* 140: 1661-1678.

Dwivedi S, Purohit P, Sharma P 2019. MicroRNAs and diseases: Promising biomarkers for diagnosis and therapeutics. *Indian J Clin Biochem*, 34: 243-245.

El-Shetry M, Mahfouz R, Frere AF et al. 2021. The interplay between atrial fibrillation and acute myocardial infarction. *Br J Hosp Med,* 82: 1-9.

Gulati R, Behfar A, Narula J et al. 2020. Acute myocardial infarction in young individuals. *Mayo Clin Proc,* 95: 136-156.

Guo JF, Zhang Y, Zheng QX et al. 2018. Association between elevated plasma microRNA-223 content and severity of coronary heart disease. *Scand J Clin Lab Invest*, 78: 373-378.

Higashi K, Yamada Y, Minatoguchi S et al. 2015. MicroRNA-145 repairs infarcted myocardium by accelerating cardiomyocyte autophagy. *Am J Physiol Heart Circ Physiol*, 309: H1813-H1826.

Hu S, Cao S, Tong Z et al. 2018. FGF21 protects myocardial ischemia-reperfusion injury through reduction of

miR-145-mediated autophagy. *Am J Transl Res*, 10: 3677-3688.
Lei Z, Wahlquist C, El Azzouzi H et al. 2021. miR-132/212 Impairs cardiomyocytes contractility in the failing heart by suppressing SERCA2a. *Front Cardiovasc Med*, 8: 592362.
Li P, Li SY, Liu M et al. 2019. Value of the expression of miR-208, miR-494, miR-499 and miR-1303 in early diagnosis of acute myocardial infarction. *Life Sci*, 32: 116547.
Liu W, Lin W, Yu L 2022. Long non-coding RNA muscleblind like splicing regulator 1 antisense RNA 1 (LncRNA MBNL1-AS1) promotes the progression of acute myocardial infarction by regulating the microRNA-132-3p/SRY-related high-mobility-group box 4 (SOX4) axis. *Bioengineered*, 13: 1424-1435.
Liu X, Fan Z, Zhao T et al. 2015. Plasma miR-1, miR-208, miR-499 as potential predictive biomarkers for acute myocardial infarction: An independent study of Han population. *Exp Gerontol*, 72: 230-238.
Miki K, Imamura T 2020. Clinical implication of miRNA in acute myocardial infarction. *J Clin Lab Anal*, 34: e23491.
Nouraee N, Mowla SJ 2015. miRNA therapeutics in cardiovascular diseases: Promises and problems. *Front Genet*, 6: 232.
Pan K, Guo G, Xue X 2021. mRNA modifications: Clinical clarification and significance. *Epigenomics*, 13: 1901-1903.
Pinchi E, Frati P, Aromatario M et al. 2019. miR-1, miR-499 and miR-208 are sensitive markers to diagnose sudden death due to early acute myocardial infarction. *J Cell Mol Med*, 23: 6005-6016.
Qin Y, Yan G, Qiao Y et al. 2019. Relationship between random blood glucose, fasting blood glucose, and gensini score in patients with acute myocardial infarction. *BioMed Res Int*, 2019: 9707513.
Rampidis GP, Benetos G, Benz DC et al. 2019. A guide for Gensini Score calculation. *Atherosclerosis*, 287: 181-183.
Salemi M, Barone C, Salluzzo MG et al. 2018. Expression of miR-132 in Down syndrome subjects. *Human Cell*, 31: 268-270.
Su Q, Liu Y, Lv XW et al. 2020. LncRNA TUG1 mediates ischemic myocardial injury by targeting miR-132-3p/HDAC3 axis. *Am J Physiol Heart Circ Physiol*, 318: H332-H344.
Sun N, Meng F, Xue N et al. 2018. Inducible miR-145 expression by HIF-1a protects cardiomyocytes against apoptosis via regulating SGK1 in simulated myocardial infarction hypoxic microenvironment. *Cardiol J*, 25: 268-278.
Ueda Y, Kosugi S, Abe H et al. 2021. Transient increase in blood thrombogenicity may be a critical mechanism for the occurrence of acute myocardial infarction. *J Cardiol*, 77: 224-230.
Wang G, Wang R, Ruan Z et al. 2020. MicroRNA-132 attenuated cardiac fibrosis in myocardial infarction-induced heart failure rats. *Biosci Rep*, 40: BSR20201696.
Wang J, Xu L, Tian L et al. 2021. Circulating microRNA-208 family as early diagnostic biomarkers for acute myocardial infarction: A meta-analysis. *Medicine*, 100: e27779.
Xu H, Cao H, Zhu G et al. 2017. Overexpression of microRNA-145 protects against rat myocardial infarction through targeting PDCD4. *Am J Transl Res*, 9: 5003-5011.
Yan X, Liu J, Wu H et al. 2016. Impact of miR-208 and its target gene nemo-like kinase on the protective effect of ginsenoside Rb1 in Hypoxia/Ischemia injuried cardiomyocytes. *Cell Physiol Biochem*, 39: 1187-1195.
Zhang M, Cheng YJ, Sara JD et al. 2017. Circulating microRNA-145 is associated with acute myocardial infarction and heart failure. *Chin Med J*, 130: 51-56.
Zhao Z, Du S, Shen S et al. 2020. microRNA-132 inhibits cardiomyocyte apoptosis and myocardial remodeling in myocardial infarction by targeting IL-1β. *J Cell Physiol*, 235: 2710-2721.

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