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RESEARCH

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Correlation analysis between the expression of serum microRNA-665 and the degree of coronary artery stenosis and major adverse cardiovascular events in patients with acute myocardial infarction

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Abstract

Background The purpose of this study was to explore the expression of miR-665 in acute myocardial infarction (AMI) and evaluate its significance in the diagnosis and prognosis of AMI.

Methods 100 patients with AMI were selected as the study group and 80 healthy subjects were chosen as the control group. The levels of miR-665 were detected by reverse transcription quantitative polymerase chain reaction (RT-qPCR) in the two groups. The diagnostic value of miR-665 expression level in AMI was analyzed by the receiver operator characteristic (ROC) curve. Kaplan-Meier curve and Cox regression were used to evaluate the predictive value of miR-665 for major adverse cardiovascular events (MACEs) in patients with AMI within 30 days after percutaneous coronary intervention (PCI).

Results The serum miR-665 level of the study group was significantly lower than that of the control group. The level of miR-665 was significantly correlated with clinical indicators of patients with AMI. ROC curve showed that miR-665 has a high diagnostic value for AMI. Survival analysis showed that Gensini score and miR-665 were independent risk factors for the occurrence of MACEs within 30 days after PCI in patients with AMI.

Conclusions Abnormal decrease of serum miR-665 expression level in patients with AMI may increase the risk of MACEs occurrence after PCI.

Keywords Acute myocardial infarction, MicroRNA-665, Gensini score, Major adverse cardiovascular events

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Background

In recent years, due to changes in diet structure and the intensification of population aging, the incidence of circulatory system diseases, mainly coronary artery disease (CAD), is increasing rapidly [1]. Acute myocardial infarction is a type of CAD. Its pathological essence is coronary atherosclerosis complicated with coronary artery thrombosis, which causes different degrees of occlusion of the diseased blood vessels, leading to myocardial tissue necrosis caused by long-term imbalance of oxygen supply and demand in the coronary artery [2, 3]. AMI is an acute disease with a high mortality and disability. At present, the key to the treatment of AMI lies in accurate early diagnosis and timely revascularization, which not only reduces damage to myocardial cells, but also greatly reduces the mortality rate of patients [4]. Recently, scientists have found multiple susceptible sites and segments related to AMI through large-scale genome analysis, indicating that AMI is caused by the interaction of environment and heredity [5]. Therefore, it is of great significance to find the diagnostic and prognostic markers related to AMI.

MicroRNAs (miRNAs) are a kind of endogenous noncoding small RNAs with highly conservative characteristics, which play an important roles in regulating proliferation, development, differentiation, and inflammation [6]. MiRNAs have been proved to be regulators of key pathways such as cell adhesion and inflammation in the pathological process of coronary atherosclerosis. They are involved in the pathogenesis of atherosclerosis by regulating lipid metabolism, oxidative stress, and endothelial function [7]. A study shown that the expression level of miR-208b in peripheral blood of patients with AMI was as high as 1600 times higher than that of healthy people [8]. Another study found that miR-1 is a risk factor affecting the prognosis of AMI, which can be used to predict the prognosis of AMI [9]. MiR-665 is located in gene 14q32.2, and its abnormal expression is associated with various diseases, such as tumor cell migration and invasion, myocardial cell inflammation and fibrosis [10]. It was found that the expression of miR-665 was decreased in patients with CAD, and the ectopic expression of miR-665 could obviously inhibit the growth of vascular smooth muscle cells [11]. Wang et al. reported that overexpression of miR-665 could regulate the expression of transforming growth factor β receptor 1 (TGFBR1) and inhibit the proliferation of vascular smooth muscle cells, thus alleviate the progress of atherosclerosis [12]. However, the research data on miR-665 in AMI population are still very few.

This study aimed to investigate the correlation between the level of miR-665 and the severity of coronary artery stenosis and poor prognosis in patients with AMI, and to provide valuable research data for finding biomarkers of AMI.

Methods

Subject inclusion and exclusion criteria

This study retrospectively analyzed the relevant information of 180 participants. Among them, 100 patients with AMI who underwent PCI admitted to the cardiology department of this hospital were selected as the study objects. The relevant indexes after PCI are summarized in Supplementary Table 1. Inclusion criteria: 1). It confirms to the diagnostic criteria published in the 2012 ESC/AHA/ACC guidelines [13]; 2). Coronary angiography was carried out and confirmed. 3). First onset. The exclusion criteria are as follows: 1). Combined with cardiomyopathy and other cardiovascular diseases; 2). Patients with history of chronic heart failure and myocardial infarction; 3). Complicated with liver and kidney dysfunction, mental illness, malignant tumor; 4). Previous history of vascular reconstruction or coronary artery transplantation. In addition, 80 healthy people with age and sex matching were selected as the control group during the same period. The control group were adults from the physical examination department who had no history of cardiovascular disease, and the results of electrocardiogram and stress echocardiography showed no suspicion of coronary artery disease. Patients or their immediate family members sign informed consent. This study conforms to the Helsinki Declaration and is implemented after being reviewed and approved by the Ethics Committee of Zhangjiakou First Hospital.

Sample collection

8mL fasting venous blood was gathered from subjects after enrollment, centrifuged for 15 min at a rate of 3000 r/min at 4℃, and the serum was separated and stored in a -80℃ refrigerator for later use. The AMI patients were sub-grouped according to the Gensini score obtained by coronary angiography. Gensini scores were performed on patients based on coronary angiography results by two experienced cardiologists who were unaware of the patient's medical history and laboratory test results. Gensini scoring criteria: 0 for no coronary artery stenosis, scored 1 for 0 ~ < 26% coronary artery stenosis, scored 2 for 26% ~<51%, scored 4 for 51% ~<76%, scored 8 for 76% ~<91%, scored 16 for 91% ~<100%, and scored 32 for 100% coronary artery stenosis. The Gensini score for each AMI patient was the sum of each branch: 0–25 point is classified as mild, 26–49 is moderate, and ≥ 50 is severe.

Detection of serum miR-665 expression level

The expression level of miR-665 in serum was detected by reverse transcription-quantitative polymerase chain

reaction (RT-qPCR). Serum samples were collected and total RNA was extracted from serum by adding TRIzol reagent. The purity of RNA samples was detected by spectrophotometer, and qualified RNA specimens with absorbance of 1.8–2.1 were selected, and cDNA was synthesized from 1 μg total RNA by reverse transcription kit. After the reaction, the amplified cDNA was used as the PCR reaction template. RT-qPCR was carried out with ABI 7900 RT-qPCR and SYBR Green I fluorescence quantitative kit. All the reactions were performed using 2 multiple Wells. U6 was specified as the internal reference, the relative miR-665 expression was calculated according to the $2^{-\triangle\triangle Ct}$ method, where $\triangle Ct = Ct_{miR-665} - Ct_{U6}$.

Study end point and follow-up

According to the prognosis of patients within 30 days after therapy, the patients were divided into two groups: good prognosis group ($n=26$) and poor prognosis group ($n=74$). The poor prognosis was defined as the occurrence of major adverse cardiovascular events (MACEs) within 30 days after surgery, such as sudden cardiac death, thrombosis, hospitalization for heart failure, atrial ventricular block, and angina recurrence. The good prognosis group was defined as no such MACEs within 30 days after surgery.

Table 1 Comparison of subjects' baseline data

Characteristics	Control group ($n=80$)	AMI group ($n=100$)	*P*
Sex (Male/Female)	45/35	58/42	0.480
Age (Years)	58.64 ± 7.08	59.27 ± 6.36	0.530
BMI (kg/m^2)	22.15 ± 3.16	22.73 ± 2.97	0.446
Smoking history (n, %)	38 (47.5%)	49 (49.0%)	0.493
Drinking history (n, %)	43 (53.8%)	55 (55.0%)	0.459
Hypertension (n, %)	/	50 (50.0%)	/
Diabetes (n, %)	/	22 (22.0%)	/
Dyslipidemia (n, %)	/	48 (48.0%)	/
Gensini score	/	25.56 ± 17.24	/
SBP (mmHg)	121.62 ± 10.79	136.61 ± 13.16	< 0.001
DBP (mmHg)	74.49 ± 6.85	85.83 ± 6.91	< 0.001
FBG (mmol/L)	4.77 ± 0.92	5.81 ± 2.20	< 0.001
TC (mmol/L)	4.17 ± 0.81	4.36 ± 0.69	0.090
TG (mmol/L)	1.41 ± 0.52	1.88 ± 0.76	< 0.001
LDL-C (mmol/L)	2.43 ± 0.74	2.93 ± 0.98	< 0.001
HDL-C (mmol/L)	1.67 ± 0.41	1.41 ± 0.70	0.003
cTnI (ng/mL)	0.02 ± 0.01	8.96 ± 4.61	< 0.001
Medication (n, %)			
β-receptor blockers	/	71 (71%)	/
Statins	/	96 (96%)	/
Antiplatelet drugs	/	97 (97%)	/
ACEI/ARB	/	69 (69%)	/
Calcium antagonists	/	19 (19%)	/

Abbreviations: AMI: acute myocardial infarction; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; TC: total cholesterol; TG: triglyceride; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; cTnI: cardiac troponin I. $P<0.05$ means a significant difference

Statistical analysis

SPSS 22.0 software was used for data processing. The Kolmogorov-Smirnov test was used to evaluate the normality of the data. The measurement data conforming to normal distribution were expressed as mean ± standard deviation (SD), and *t*-test was used for inter-group comparison. Counting data was represented by n, and Chi-square test was used for comparison between groups. The correlation between miR-665 expression level and clinical indicators was examined by Pearson method. The diagnostic value of serum miR-665 in AMI was evaluated by receiver operator characteristic (ROC) curve. The patients were divided into miR-665 high expression group and miR-665 low expression group according to the mean level of miR-665. Kaplan-Meier method was applied to draw the survival curve, and the Log-rank test was used to compare the prognosis differences between the two groups. $P<0.05$ means significant differences.

Results

Comparison of baseline data between the two groups

The general data of these two groups are summarized in Table 1. There were no significant differences in gender, age, body mass index (BMI), total cholesterol (TC), smoking history and drinking history in two groups ($P>0.05$). There were significant differences in systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood glucose (FBG), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and cardiac troponin I (cTnI) between the two groups ($P<0.05$).

The expression level of serum miR-665 and its value in clinical diagnosis of AMI

The serum level of miR-665 was determined by RT-qPCR, and the results revealed that the level of miR-665 in patients with AMI was significantly lower than that in the control group (Fig. 1A, $P<0.001$). Further, the ROC curve was established to evaluate the diagnostic significance of miR-665 in AMI. Figure 1B showed that the area under the curve (AUC) value of this curve is 0.909, and the sensitivity and specificity are 82.5% and 88.0%, respectively, which indicats that the diagnostic accuracy of miR-665 for AMI is high.

Expression of miR-665 in different degrees of coronary artery disease

According to the Gensini score, AMI patients were grouped into mild ($n=41$), moderate ($n=39$) and severe group ($n=20$). The results showed that compared with the mild group, the level of miR-665 in the moderate and

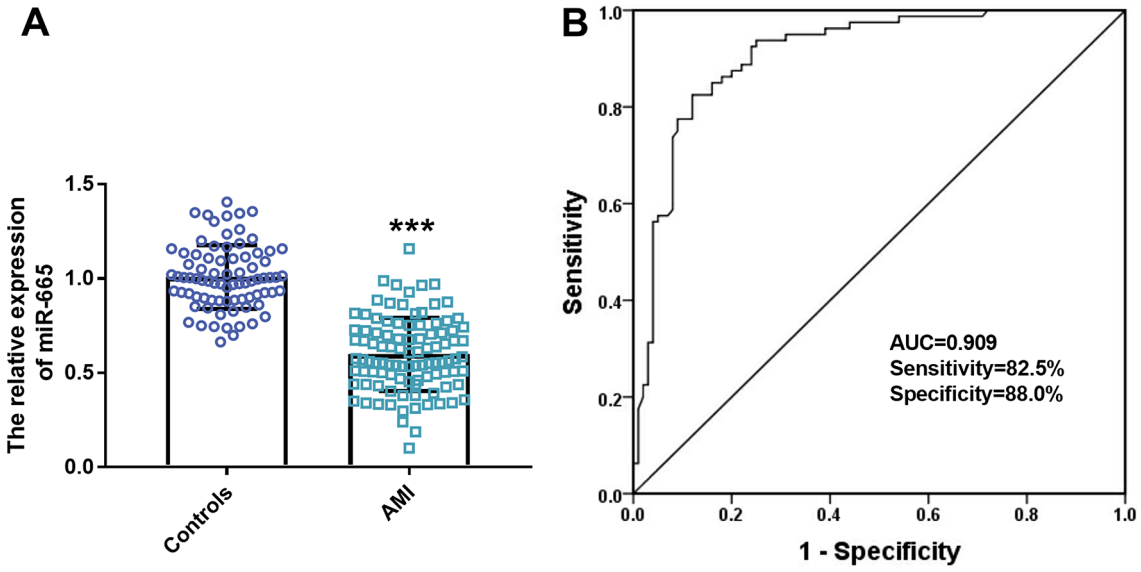

Fig. 1 The expression level of miR-665 in the serum of patients with AMI and its clinical diagnostic value in AMI. **A**. The level of serum miR-665 was down-regulated in AMI patients. **B**. The AUC value of ROC curve was 0.909, and the sensitivity and specificity were 82.5% and 88.0%, respectively. $^{***}P<0.001$ vs. Controls. Abbreviations: AMI, acute myocardial infarction; ROC, receiver operator characteristic; AUC, area under the curve

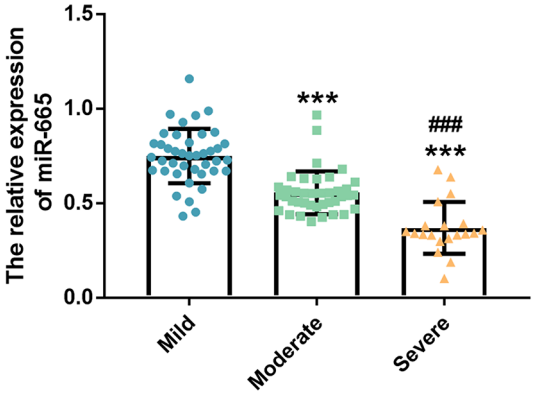

Fig. 2 Expression levels of miR-665 under different Gensini scores. $^{***}P<0.001$ vs. mild group. $^{\#\#\#}P<0.001$ vs. moderate group

Table 2 Correlation between miR-665 and clinical indicators

Clinical indicators	*r*	*P*
SBP (mmHg)	-0.531	< 0.001
DBP (mmHg)	-0.493	< 0.001
FBG (mmol/L)	-0.325	0.026
TC (mmol/L)	-0.201	0.087
TG (mmol/L)	-0.608	< 0.001
HDL-C (mmol/L)	0.396	0.011
LDL-C (mmol/L)	-0.655	< 0.001
cTnI (ng/mL)	-0.701	< 0.001
Gensini score	-0.687	< 0.001

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; cTnI: cardiac troponin I. $P<0.05$ means significant difference

severe groups was significantly decreased. In addition, compared with the moderate group, the level of miR-665 in the severe group was lower (Fig. 2, $P<0.001$). The above results indicated that the expression level of miR-665 decreased gradually with the severity of the disease.

Correlation between miR-665 level and clinical indicators in AMI patients

Pearson correlation coefficient was used to evaluate the correlation between miR-665 and clinical indicators in patients with AMI, and the results were shown in Table 2. Results suggested that SBP, DBP, TG, LDL-C, cTnI and Gensini were strongly negatively correlated with the level of miR-665 in patients with AMI ($P<0.001$). There was a moderate negative correlation between FBG and miR-665 ($P<0.05$). In addition, HDL-C was positively correlated with the level of miR-665 ($P<0.05$).

Follow-up analysis

On the basis of the mean value of miR-665, patients with AMI were divided into miR-665 high expression group ($n=50$) and miR-665 low expression group ($n=50$). Six patients in the high miR-665 expression group developed MACEs within 30 days after PCI surgery, while 20 cases in the low miR-665 expression group had MACEs (Table 3, $P<0.01$). As shown in Fig. 3, Kaplan-Meier curve showed that low expression of miR-665 increased the risk of poor prognosis in patients with AMI ($P<0.05$). As shown in Table 4, Cox regression analysis showed that Gensini score (HR=7.818, 95% CI=1.821–33.574, $P=0.006$) and miR-665 (HR=0.245, 95% CI=0.068–0.878, $P=0.030$) were independent factors influencing

Table 3 The number of patients with AMI who developed MACEs within 30 days after surgery

MACEs	miR-665 high expression ($n=50$)	miR-665 low expression ($n=50$)	*P*
Cardiogenic shock (n)	0	3	
Sudden cardiac death (n)	0	1	
Thrombosis (n)	1	4	
Heart failure (n)	2	2	
Atrial ventricular block (n)	2	5	
Angina recurrence (n)	1	5	
Total (n, %)	6	20	0.002

Abbreviations: MACEs, major adverse cardiovascular events. $P<0.05$ means significant differences

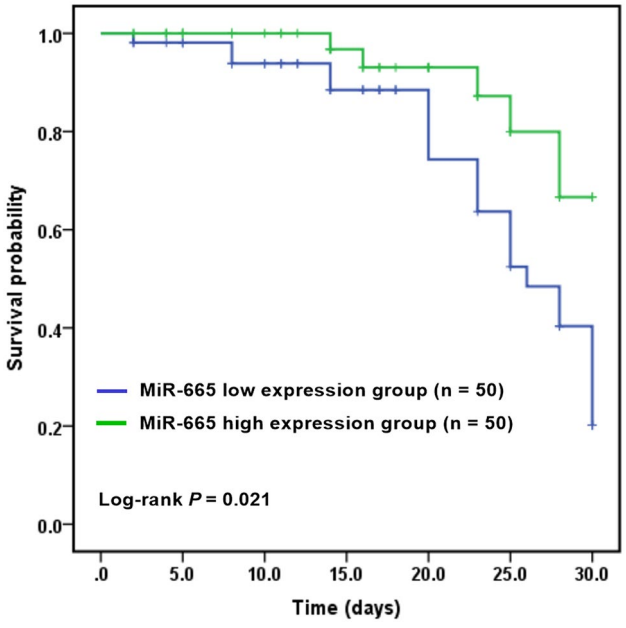

Fig. 3 Kaplan-Meier curve of MACEs incidence in AMI patients within 30 days after surgery. Abbreviations: MACEs, major adverse cardiovascular events; AMI, acute myocardial infarction

the occurrence of MACEs in AMI patients within 30 days after surgery.

Discussion

AMI is one of the most threatening cardiovascular emergencies. Due to its sudden onset, dangerous condition, rapid progression, high mortality and disability rate, it has become the main cause of endangering people's health and life safety all over the world [14]. This is particularly prominent in developing countries with relatively backward economic and medical strength, so accurate and early diagnosis is crucial to control disease development, limit myocardial damage and protect heart function [15]. This study demonstrated that the expression level of serum miR-665 showed an obvious downward trend in patients with AMI, and further ROC curve

Table 4 Multivariate COX analysis

Items	Multivariate analysis		
	HR	95% CI	*P*
Sex (Male/Female)	0.593	0.195–1.798	0.356
Age (Years)	0.712	0.226–2.178	0.418
BMI (kg/m2)	0.951	0.315–2.869	0.929
Smoking history (n, %)	1.377	0.339–5.588	0.655
Drinking history (n, %)	0.644	0.223–1.858	0.416
Hypertension (n, %)	1.133	0.307–4.187	0.851
Diabetes (n, %)	0.799	0.157–4.054	0.786
Dyslipidemia (n, %)	0.693	0.202–2.374	0.559
SBP (mmHg)	2.901	0.934–9.015	0.067
DBP (mmHg)	2.277	0.927–8.288	0.181
TC (mmol/L)	1.412	0.410–4.869	0.584
TG (mmol/L)	0.908	0.354–2.333	0.539
HDL-C (mmol/L)	0.427	0.148–1.236	0.117
LDL-C (mmol/L)	1.697	0.571–5.042	0.341
FBG (mmol/L)	0.699	0.223–2.190	0.842
Gensini score	7.818	1.821–33.574	0.006
cTnI (ng/mL)	3.449	0.954–12.446	0.059
MiR-665	0.245	0.068–0.878	0.030

Abbreviations: AMI: acute myocardial infarction; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; TC: total cholesterol; TG: triglyceride; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; cTnI: cardiac troponin I. $P<0.05$ means a significant difference

analysis showed that miR-665 had the ability to distinguish AMI from healthy individuals. In addition, Pearson analysis indicated that the miR-665 level was significantly correlated with the degree of coronary artery stenosis in patients with AMI. In a 30-day follow-up analysis, it was found that the low expression of miR-665 was closely related to the poor prognosis in patients with AMI after PCI.

Recently, with the development of pathophysiology of the circulatory system, the application and influence of miRNA in cardiovascular diseases have been gradually revealed. At present, related studies have confirmed that miRNA may be involved in the pathogenesis of cardiovascular diseases such as CAD [16, 17]. As reported by Rawat et al., miRNA plays an indispensable role in promoting cell proliferation, differentiation and apoptosis, and it can supply a new direction for the clinical first-line evaluation of the severity of cardiomyopathy [18]. In terms of prognosis, some scholars have pointed out that circulating miR-1 level within 3 h of chest pain has potential diagnostic value for AMI and is an independent risk factor affecting the prognosis of AMI [19]. In terms of mechanism, Yu et al. reported that miR-133 can protect cardiomyocytes from invasion of myocardial infarction [20]. Therefore, circulating miRNAs have the potential to be powerful diagnostic or prognostic markers for a variety of cardiovascular diseases under different physiological and pathological conditions. In this study, it was learned that miR-665 is up-regulated in the serum of

patients with AMI. As for miR-665, which is the focus of this study, some scholars have previously proposed that it is related to cardiovascular diseases such as heart failure, AMI and atherosclerosis, and it may become a circulating biomarker for the diagnosis of heart failure [10, 21]. We further verified this in this experiment. First of all, it was observed that serum miR-665 level in the AMI group was significantly lower than that in the healthy control group, which was consistent with the expected data analysis results. As far as the traditional study of general cardiovascular clinical data is concerned, blood pressure, blood glucose and blood lipids have been proved as risk factors for cardiovascular diseases in previous studies [22]. In this experiment, general data between the two groups were compared, and it was found that there were differences in blood pressure, lipids, blood sugar, Gensini score and cTnI between the two groups, which was consistent with previous studies [23, 24].

Here, this study conducted a 30-day follow-up analysis of patients with AMI after PCI. From the Kaplan-Meier curve, it was found that the risk of poor prognosis in the group with high expression of miR-665 was significantly lower than that in the group with low expression of miR-665. Based on this, it is reasonable to speculate that miR-665 is significantly related to poor prognosis in patients with AMI. Further, Cox regression analysis showed that miR-665 and Gensini scores were independent risk factors for poor prognosis of AMI. Gensini score is usually used to assess the degree of CAD, and its good value has been confirmed in clinical practice [25]. Previous studies have confirmed that coronary artery disease with high degree of stenosis is more likely to develop into vascular occlusion and myocardial infarction, and the severity of coronary artery disease is one of the main predictors of cardiovascular adverse events and death risk [26]. In a study that included 102 AMI patients who underwent PCI, Wang et al. observed that the Gensini scores of patients with MACEs from hospitalization to 6 months after PCI were higher than that of the group without MACEs [27]. In this study, patients were divided into mild, moderate and severe disease groups according to Gensini scores. It was observed that the expression level of miR-665 decreased gradually with the deepening of severity, which further clarifying the correlation between miR-665 and the degree of coronary artery stenosis. More importantly, there was a significant negative correlation between miR-665 and Gensini scores in Pearson correlation analysis.

There are several limitations to this study. Firstly, single-center study and small sample size may lead to bias in experimental results. Therefore, multi-center experiments with larger sample size should be conducted in the future. Secondly, the short follow-up period does not represent a long-term situation. Finally, this study was an observational study, and the literature supporting miR-665 in the causes, mechanisms, plaque stability and treatment of acute myocardial infarction is insufficient, and its mechanism is still worthy of further study and verification.

In recent decades, researchers have been working to explore the mysteries of miRNAs and apply them to predict, diagnose, or treat diseases of the cardiovascular system. The death rate from AMI has not decreased in the past 10 years, which is also related to the lack of drugs available in clinical practice to prevent heart reperfusion injury. As a new type of biomarker, miRNA research in the cardiovascular field is still in its infancy and needs to be further explored. Studying the importance of miRNA in cardiovascular disease and understanding its mechanism of action will lead to better prevention and treatment of disease.

Conclusions

In summary, by analyzing the correlation between serum miR-665 level and clinical characteristics of patients with AMI, it was found that miR-665 level with relatively low expression in patients with AMI would present higher blood pressure, blood lipid, blood glucose and Gensini scores. In addition, low expression of miR-665 in patients with AMI increased the risk of poor prognosis 30 days after surgery. Therefore, it is speculated that monitoring the level of serum miR-665 can predict the occurrence of poor prognosis to some extent in the early stage of treatment of patients with AMI, which has a certain guiding role for clinical treatment and intervention.

Abbreviations

AMI	Acute myocardial infarction
RT-qPCR	Reverse transcription quantitative polymerase chain reaction
ROC	Receiver operator characteristic
MACEs	Major adverse cardiovascular events
PCI	Percutaneous coronary intervention
CAD	Coronary artery disease
miRNAs	MicroRNAs
TGFBR1	Transforming growth factor β receptor 1
BMI	Body mass index
TC	Total cholesterol

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13019-024-02998-z.

Supplementary Material 1

Acknowledgements

Not applicable.

Author contributions

Chen Wang, Jie Yang, Yujie Shi, Lining Liu made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, and draft of the manuscript. Yujie Fu revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

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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
Patients or their immediate family members sign informed consent, and this study conforms to the Declaration of Helsinki, and is implemented after review and approval by the Ethics Committee of Zhangjiakou First Hospital.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Wei ZY, Lai JY, Li YT, Yu XY, Liu YH, Hu JX, et al. Colchicine efficacy comparison at varying time points in the peri-operative period for coronary artery disease: a systematic review and meta-analysis of randomized controlled trials. Front Cardiovasc Med. 2023;10:1156980. PubMed PMID: 37600022. Pubmed Central PMCID: PMC10438985.
2. Gough B, Robertson S, Luck H. Engendered expressions of anxiety: men's Emotional communications with women and other men. Front Sociol. 2021;6:697356. PubMed PMID: 34268351. Pubmed Central PMCID: PMC8275859.
3. Cheng Z, Shi Y, Peng H, Zhao D, Fan Q, Liu J. Prognostic significance of percutaneous coronary intervention for First Acute myocardial infarction with heart failure: five-year Follow-Up results. Cardiol Res Pract. 2022;2022:5791295. PubMed PMID: 36386562. Pubmed Central PMCID: PMC9649329.
4. Zhai C, Li R, Hou K, Chen J, Alzogool M, Hu Y, et al. Value of blood-based microRNAs in the diagnosis of Acute myocardial infarction: a systematic review and Meta-analysis. Front Physiol. 2020;11:691. PubMed PMID: 32922300. Pubmed Central PMCID: PMC7456928.
5. Li H, Yang H, Wang D, Zhang L, Ma T. Peroxiredoxin2 (Prdx2) reduces oxidative stress and apoptosis of myocardial cells Induced by Acute myocardial infarction by inhibiting the TLR4/Nuclear factor kappa B (NF-kappaB) signaling pathway. Med Sci Monit. 2020;26:e926281. PubMed PMID: 33268762. Pubmed Central PMCID: PMC7722772.
6. Chen C, Jiang J, Fang M, Zhou L, Chen Y, Zhou J, et al. MicroRNA-129-2-3p directly targets Wip1 to suppress the proliferation and invasion of intrahepatic cholangiocarcinoma. J Cancer. 2020;11(11):3216–24. PubMed PMID: 32231727. Pubmed Central PMCID: PMC7097937.
7. Baldan A, Fernandez-Hernando C. Truths and controversies concerning the role of miRNAs in atherosclerosis and lipid metabolism. Curr Opin Lipidol. 2016;27(6):623–9. PubMed PMID: 27755115. Pubmed Central PMCID: PMC5465636.
8. Corsten MF, Dennert R, Jochems S, Kuznetsova T, Devaux Y, Hofstra L, et al. Circulating MicroRNA-208b and MicroRNA-499 reflect myocardial damage in cardiovascular disease. Circ Cardiovasc Genet. 2010;3(6):499–506. PubMed PMID: 20921333.
9. Wang L, Jin Y. Noncoding RNAs as biomarkers for Acute Coronary Syndrome. Biomed Res Int. 2020;2020:3298696. PubMed PMID: 32337239. Pubmed Central PMCID: PMC7154975.
10. Fan J, Zhang X, Nie X, Li H, Yuan S, Dai B, et al. Nuclear miR-665 aggravates heart failure via suppressing phosphatase and tensin homolog transcription. Sci China Life Sci. 2020;63(5):724–36. PubMed PMID: 31664601.
11. Wang L, Zhou J, Guo F, Yao T, Zhang L. MicroRNA-665 regulates cell proliferation and apoptosis of vascular smooth muscle cells by targeting TGFBR1. Int Heart J. 2021;62(2):371–80. PubMed PMID: 33731513.
12. Yan T, Zhu S, Zhu M, Zhu K, Dong L, Wang C, et al. Clinical performance of a Powered Surgical Stapler for Left Atrial Appendage Resection in a video-assisted thoracoscopic ablation for patients with Nonvalvular Atrial Fibrillation. Int Heart J. 2021;62(4):764–70. PubMed PMID: 34276010.
13. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. Glob Heart. 2012;7(4):275–95. PubMed PMID: 25689940.
14. Han X, Bai L, Jeong MH, Ahn JH, Hyun DY, Cho KH, et al. Higher long-term mortality in patients with Non-ST-Elevation myocardial infarction than ST-Elevation myocardial infarction after Discharge. Yonsei Med J. 2021;62(5):400–8. PubMed PMID: 33908210. Pubmed Central PMCID: PMC8084695.
15. Tin NT, Van Minh H, Thang DC, Phuong PTM. Serum periostin levels in Acute myocardial infarction patients: a 3-month follow-up study. Acta Inf Med. 2023;31(3):195–9. PubMed PMID: 37781497. Pubmed Central PMCID: PMC10540933.
16. Kaneto CM, Nascimento JS, Prado M, Mendonca LSO. Circulating miRNAs as biomarkers in cardiovascular diseases. Eur Rev Med Pharmacol Sci. 2019;23(5):2234–43. PubMed PMID: 30915771.
17. Cavarretta E, Frati G. MicroRNAs in Coronary Heart Disease: ready to enter the clinical Arena? Biomed Res Int 2016;2016:2150763. PubMed PMID: 27882321. Pubmed Central PMCID: PMC5110879.
18. Rawat M, Kadian K, Gupta Y, Kumar A, Chain PSG, Kovbasnjuk O et al. MicroRNA in Pancreatic Cancer: from Biology to therapeutic potential. Genes (Basel). 2019;10(10). PubMed PMID: 31557962. Pubmed Central PMCID: PMC6827136.
19. Su T, Shao X, Zhang X, Yang C, Shao X. Value of circulating miRNA-1 detected within 3 h after the onset of acute chest pain in the diagnosis and prognosis of acute myocardial infarction. Int J Cardiol. 2020;307:146–51. PubMed PMID: 31611081.
20. Yu Y, Liu H, Yang D, He F, Yuan Y, Guo J, et al. Aloe-Emodin attenuates myocardial infarction and apoptosis via up-regulating miR-133 expression. Pharmacol Res. 2019;146:104315. PubMed PMID: 31207343.
21. Zhang Y, Liang Q, Zhang Y, Hong L, Lei D, Zhang L. Olmesartan alleviates bleomycin-mediated vascular smooth muscle cell senescence via the miR-665/SDC1 axis. Am J Transl Res. 2020;12(9):5205–20. PubMed PMID: 33042414. Pubmed Central PMCID: PMC7540088.
22. Navarro-Vidal B, Banegas JR, Leon-Munoz LM, Rodriguez-Artalejo F, Graciani A. Achievement of cardiometabolic goals among diabetic patients in Spain. A nationwide population-based study. PLoS ONE. 2013;8(4):e61549. PubMed PMID: 23637851. Pubmed Central PMCID: PMC3630125.
23. Negi S, Neupane D, Sahoo SK, Mahajan T, Swaroop K, Moran AE, et al. Prices of combination medicines and single-molecule antihypertensive medicines in India's private health care sector. J Clin Hypertens (Greenwich). 2021;23(4):738–43. PubMed PMID: 33369089. Pubmed Central PMCID: PMC8678655.
24. Al Aqeel A, Mojiminiyi OA, Al Dashti R, Al Ozairi ES. Differences in physician compliance with guideline on lipid profile determination within 24 h after acute myocardial infarction. Med Princ Pract. 2005 Jan-Feb;14(1):41–5. PubMed PMID: 15608480.
25. Nursalim A, Suryaatmadja M, Panggabean M. Potential clinical application of novel cardiac biomarkers for acute myocardial infarction. Acta Med Indones. 2013;45(3):240–50. PubMed PMID: 24045397.
26. Kleczynski P, Legutko J, Rakowski T, Dziewierz A, Siudak Z, Zdzienicka J, et al. Predictive utility of NT-pro BNP for infarct size and left ventricle function after acute myocardial infarction in long-term follow-up. Dis Markers. 2013;34(3):199–204. PubMed PMID: 23334649. Pubmed Central PMCID: PMC3809970.
27. Wang KY, Zheng YY, Wu TT, Ma YT, Xie X. Predictive value of Gensini score in the long-term outcomes of patients with coronary artery Disease who underwent PCI. Front Cardiovasc Med. 2021;8:778615. PubMed PMID: 35141291. Pubmed Central PMCID: PMC8818732.

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