Journal of Cardiothoracic Surgery

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Downregulation of serum miR-30c-5p serves as a biomarker to predict disease onset and short-term prognosis in acute coronary syndrome patients

Bo Chang[1†], Xiangfeng Zhang[2†], Riliang Fang[3], Huibin Li[3*], Youdan Zhou[3] and Yakun Wang[4*]

Abstract

Background & objective Timely intervention for Acute coronary syndrome (ACS) could effectively reduce the mortality rate of ACS patients. This study aimed to investigate the clinical significance of miR-30c-5p for ACS and to provide a convenient biomarker for diagnosing of ACS.

Methods Baseline information was collected from a total of 173 subjects (98 ACS subjects and 65 healthy subjects). The miR-30c-5p expression was evaluated by the Polymerase chain reaction (PCR). The predictive value of miR-30c-5p for ACS was assessed by Receiver Operating Characteristic (ROC) curve and multivariate logistic regression analysis. The relationship between miR-30c-5p expression and ACS severity was assessed by correlation analysis. Furthermore, the prognostic value of miR-30c-5p on Major Adverse Cardiovascular Events (MACE) occurrence was assessed by the Kaplan-Meier (K-M) curve to evaluate its prognostic significance.

Results Downregulation of miR-30c-5p was observed in ACS subjects and its diagnostic value on ACS was confirmed by the ROC curve. MiR-30c-5p could also discriminate acute myocardial infarction (AMI) from unstable angina pectoris (UAP) subjects in ACS. The expression of miR-30c-5p was negatively correlated with the cardiac troponin I (cTnI) levels and the Gensini score. A lower miR-30c-5p expression was observed in ACS subjects who developed MACE ($P=0.020$), and the K-M curve further confirmed the close correlation between miR-30c-5p expression and MACE occurrence in ACS. MiR-30c-5p was also identified as an independent prognostic factor for MACE in ACS.

Conclusions Serum miR-30c-5p expression was correlated with the severity of ACS, and downregulated miR-30c-5p expression showed a diagnostic and prognostic value in ACS.

Keywords ACS, MACE, miR-30c-5p, Risk factor, Prognosis

[†]Bo Chang and Xiangfeng Zhang contributed equally to this work.

*Correspondence:
Huibin Li
lihuibin9633@163.com
Yakun Wang
yakunwang147@163.com
[1]Department of Cardiology, The Sixth People's Hospital of Nantong, Nantong 226001, China
[2]Department of Internal Medicine, Shanghai Hospital of PAP, Shanghai 201103, China
[3]Department of Cardiovascular Medicine, The First People's Hospital of Xiaoshan District, No. 199 Shi Xin Nan Lu, Xiaoshan District, Hangzhou 311200, China
[4]Department of Intensive Care Medicine, Hangzhou TCM, Hospital Affiliated to Zhejiang Chinese Medicine University, No.1630, Huanding Road, Shangcheng District, Hangzhou 310044, China

Introductions

Acute coronary syndrome (ACS) represents a severe category of coronary heart disease (CHD), with a high mortality rate and prevalence [1]. With the improvement of early prevention and treatment, the incidence and mortality of ACS in some countries and regions have decreased but remain at a high level [2]. The population of ACS population continues to rise annually in China [3]. ACS comprises two types: unstable angina pectoris (UAP) and acute myocardial infarction (AMI) which can be categorized as ST-elevation and non-ST-elevation. ACS typically occurs when coronary artery plaque ruptures due to internal and external stimuli, forming a thrombus that blocks coronary artery branches [4]. AMI is usually accompanied by excessive inflammation, cellular oxidative stress, cell apoptosis, fibrosis, reactive hypertrophy, and other pathological processes involved in the myocardial status after coronary blood reperfusion [5]. Without timely intervention, it will further lead to ischemic injury and even necrosis of cardiomyocytes, which seriously threaten the lives of ACS patients. Additionally, the incidence of MACE should also be effectively monitored in ACS patients who underwent percutaneous coronary intervention (PCI) as the risk of MACE still existed in ACS patients after PCI. Therefore, early, accurate, and effective diagnosis and prognosis are the key links to the clinical management of ACS.

MicroRNAs (miRNAs) are small, single-stranded, noncoding RNAs that are expressed endogenously, usually consisting of 19–22 nucleotide sequences [6]. In recent years, miRNAs have emerged as a prominent area of focus and investigation across a range of research disciplines. Up to now, more than 1,800 unique miRNAs have been identified, and many of them could inhibit or promote the progression of ACS [7, 8]. For instance, miR-126 and miR-21 were both upregulated in ACS and could serve as the diagnostic biomarkers for ACS [9]. Serum miRNA-499 and miRNA-210 were also upregulated in ACS patients and showed potential diagnostic value in ACS progression [10]. MiR-30c-5p was involved in the inflammatory response of cerebral ischemia-reperfusion injury [11] and as the progression of ACS is also associated with excessive inflammation, miR-30c-5p may play an essential role in the inflammatory process of ACS. Moreover, miR-30c-5p was reported to be downregulated in atherosclerosis which can lead to ACS if left untreated [12]. A neural network study screening for ACS-related miRNAs found 34 dysregulated miRNAs, with miR-30c-5p showing a strong correlation to ACS [13].

Based on the above information, we could figure out that miR-30c-5p should be associated with the progression of ACS, leading to the hypothesis that miR-30c-5p might be considered as a potential biomarker for ACS. In this study, we analyzed the expression levels of miR-30c-5p in participants and assessed its clinical significance in ACS by evaluating its potential diagnostic and prognostic value.

Subjects and methods

Clinical subjects

A total of 173 subjects including 98 subjects with chest pain and diagnosed with ACS (ACS group: 31 subjects with UAP and 68 subjects with AMI) and 65 healthy individuals (HC group) underwent coronary arteriography at The First People's Hospital of Xiaoshan District from January 2022 to December 2023. The Ethics Review Committee of The First People's Hospital of Xiaoshan District approved this research. The informed consent was signed by all subjects or their families after the purpose of this research was notified.

Inclusion criteria for subjects were: (1) the age of all patients should be over 18 years old and under 80 years old; (2) the chest pain of the patients less than 24 h; (3) patients' clinical data were complete; (4) patient met the ACS diagnostic criteria of American College of Cardiology and European Society of Cardiology [14].

The exclusion criteria for subjects were: (1) patients with any immune deficiency diseases; (2) patients who have undergone cardiac surgery or antithrombotic therapy; (3) patients with various infectious diseases, hemorrhagic diseases, and severe anemia; (4) patients with any malignant tumor; (5) patients with serve liver and kidney dysfunctions; 6)patients who were pregnant or lactating.

Baseline information and blood collection

General information including age, gender, and BMI were collected and recorded. Disease history of type 2 diabetes mellitus (T2DM), hypertension (HBP), hyperlipidemia (HLP), smoking, and drinking were also documented.

The fasting blood samples were taken from all subjects the next morning after hospitalization and then the serum of the blood sample was collected after centrifuging at 3700 rpm for 20 min. The serum was stored at -80 °C for later analysis. The blood indicators including fasting blood glucose (FBG), white blood cell count (WBC), platelets (PLT), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), creatine kinase isoenzymes MB (CK-MB), cardiac troponin (cTnI), and high-sensitivity C-reactive protein (hs-CRP) were analyzed by an automatic biochemical analyzer (Roche Cobas 8000, Germany). Additionally, the Gensini Score of all ACS subjects was calculated.

Analysis of the expression level of miR-30c-5p

Total RNA extraction of the serum samples from all subjects was conducted with the help of TRIzol reagent (Sigma, USA), and the purity and concertation of the

extracted RNA were analyzed by NanoDrop-2000 (Thermo Fisher Scientific, USA). Then the extracted RNA was transcribed into cDNA by using the TaqMan MicroRNA reverse transcription kit. The quantification of miR-30c-5p was analyzed by the 7300 RT-PCR system (Applied Biosystems, USA) with the help of the SYBR kit (Invitrogen, USA). The sequences of the primers were listed as follows: miR-30c-5p forward: 5'-AGCGTCGTAT CCAGTGCAAT-3', miR-30c-5p reverse: 5'-GTCGTATC CAGTGCGTGTCG-3'; cel-miR-39 forward: 5'-UCACC GGGUGAAAUCAGCUUG-3', cel-miR-39 reverse: 5'-TG CTCAGCAGCACACTGT-3'. The Eq. $2^{-\Delta\Delta Ct}$ was utilized to calculate the expression level of miR-30c-5p and normalized with miR-39.

Prognosis analysis of ACS subjects

A six-month follow-up study was conducted on subjects with ACS by subsequent visit and telephone consultations. The occurrences of MACE (death, cardiogenic shock, recurrent myocardial infarction, angina, revascularization, heart failure) and the survival status of ACS subjects were recorded. Potential independent prognostic factors for MACE were analyzed by the multivariate COX regression analysis. The relationship between miR-30c-5p expression and the prognosis of ACS subjects was also assessed Kaplan-Meier curve.

Table 1 Comparison of baseline information between the healthy control group and ACS group

Indicators	HC group ($n=65$)	ACS group ($n=98$)	*P*-value
Age (years)	56.65 ± 7.43	57.56 ± 10.45	0.542
Gender (male)	41 (63.08%)	59 (60.20%)	0.712
BMI (kg/m2)	22.23 ± 1.93	22.64 ± 2.24	0.228
T2DM	20 (30.77%)	21 (21.43%)	0.178
HBP	7 (10.77%)	21 (21.43%)	0.077
HLP	10 (15.38%)	26 (26.53%)	0.093
Drink	28 (43.08%)	36 (36.73%)	0.417
Smoke	22 (33.85%)	47 (47.96%)	0.074
WBC ($1*10^9$/L)	**7.03 ± 1.34**	**7.82 ± 1.74**	**0.002***
PLT ($1*10^9$/L)	**202.99 ± 17.51**	**211.13 ± 21.39**	**0.012***
CK-MB (U/L)	**15.67 ± 3.03**	**18.98 ± 6.70**	**0.0003***
TC (mmol/L)	4.29 ± 0.62	4.52 ± 0.93	0.092
TG (mmol/L)	**1.52 ± 0.27**	**1.66 ± 0.50**	**0.033***
HDL-C (mmol/L)	**1.10 ± 0.22**	**1.05 ± 0.10**	**0.044***
LDL-C (mmol/L)	**2.82 ± 0.31**	**3.02 ± 0.58**	**0.012***
FBG (mmol/L)	5.20 ± 0.82	5.33 ± 0.41	0.182
cTnI (μg/L)	-	1.48 ± 1.15	-
hs-CRP (mg/L)	-	6.49 ± 0.79	-
GS	-	50.65 ± 15.30	-

Note *$P<0.05$. BMI: body mass index; T2DM: type II diabetes mellitus; HBP: hypertension; HLP: hyperlipidemia; WBC: white blood cells; PLT: platelet; CK-MB: creatine kinase isoenzymes - MB; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FBG: fasting blood glucose; cTnI: cardiac troponin I; hs-CRP: hypersensitive C-reactive protein; NT-proBNP: N-terminal B-type natriuretic peptide precursor; GS: Gensini score

Statistical analysis

Software of SPSS and GraphPad Prism were utilized to analyze the data and create the diagrams. The results were presented as mean value ± SD. The chi-square test and t-test were employed to analyze the differences between the two groups. The Pearson correlation analysis was utilized to assess the relationship between miR-30c-5p expression and the levels of cTnI and Gensini in ACS. The diagnostic value of miR-30c-5p for ACS was evaluated by a receiver operating characteristic (ROC) curve. Multivariate logistic regression analysis was used to explore the risk factors for ACS, and the independent prognostic factors for MACE in ACS subjects were assessed by multivariate COX regression analysis. The association between miR-30c-5p expression and the prognosis of ACS subjects was assessed by the Kaplan-Meier survival curve. $P<0.05$ was considered as significant.

Results

Comparison of general information

The baseline information of all subjects was collected and recorded in Table 1. Significant differences were observed among the levels of WBC, PLT, CK-MB, TG, HDL-C, and LDL-C in ACS subjects compared with HC groups ($P<0.05$). The levels of WBC, PLT, CK-MB, TG, and LDL-C in ACS subjects were obviously increased while the level of HDL-C was decreased compared with healthy individuals. There was no significant difference among age, gender, BMI, history of T2DM /HBP /HLP / drinking /smoking, TC, and FBG levels in ACS subjects compared with the HC group ($P>0.05$).

The expression level of miR-30c-5p and the ROC analysis

The miR-30c-5p expression of all the subjects was presented in Fig. 1. The expression level of miR-30c-5p was significantly downregulated in the ACS group compared with the HC group ($P<0.0001$, Fig. 1, A). Subjects in the ACS groups could be categorized into the AMI group and the UAP group. A notable low expression of miR-30c-5p was observed in the AMI group compared with the UAP group ($P<0.0001$, Fig. 1, B).

The ROC curve was performed to verify the pedictive value of miR-30c-5p on ACS (Fig. 2). According to Fig. 2, A, miR-30c-5p showed a significant diagnostic value for ACS with an AUC value of 0.883 (95% CI = 0.824–0.942, $P<0.0001$), and the sensitivity and specificity for distinguishing the ACS from healthy individuals was 74.63% and 90.77%, respectively. MiR-30c-5p could also differentiate AMI subjects from UAP subjects (Fig. 2, B). The AUC value was 0.783 (95% CI = 0.694–0.872, $P<0.0001$) with a sensitivity of 74.63% and specificity of 74.19%.

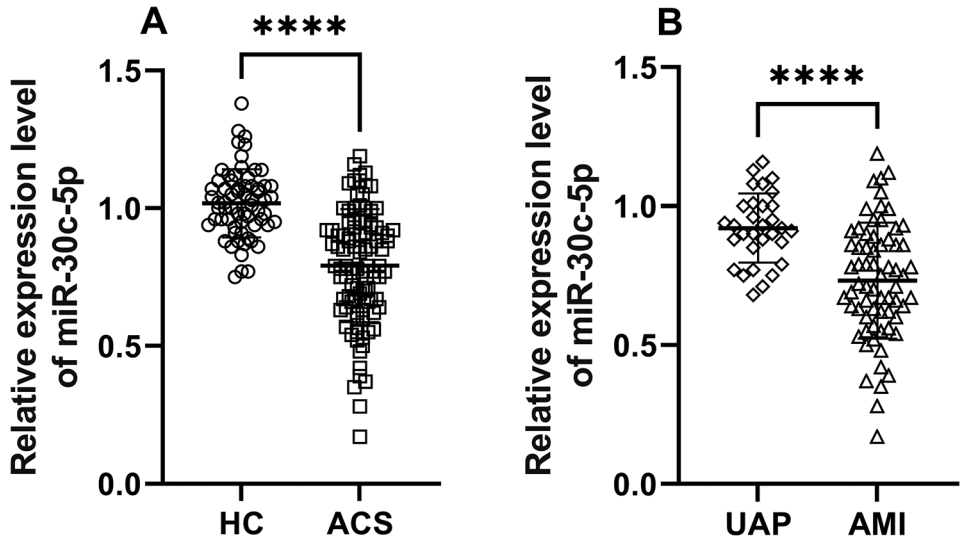

Fig. 1 The miR-30c-5p expression levels in the subjects. (**A**) the miR-30c-5p expression was notably downregulated in acute coronary syndrome subjects compared with healthy individuals. (**B**) the expression level of miR-30c-5p in acute myocardial infarction subjects was significantly downregulated compared with the unstable angina pectoris group. ****$P < 0.0001$

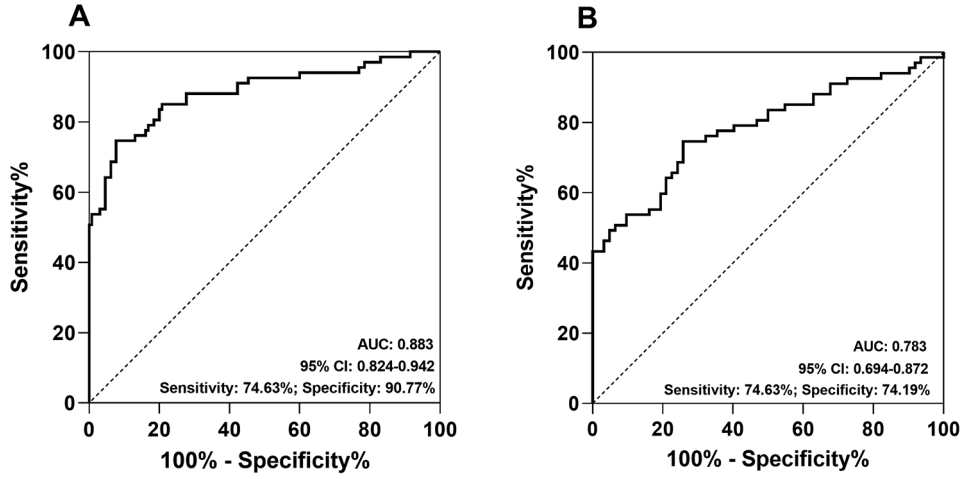

Fig. 2 The ROC curve of miR-30c-5p on diagnosing acute coronary syndrome. MiR-30c-5p showed a diagnostic value in differentiating acute coronary syndrome from healthy individuals (**A**) and distinguishing acute myocardial infarction from unstable angina pectoris (**B**)

Correlation between miR-30c-5p expression and severity of ACS

The association between miR-30c-5p expression and ACS severity was evaluated by a correlation analysis. MiR-30c-5p was negatively correlated with the cTnI levels with a correlation coefficient r = -0.543 ($P<0.0001$, Fig. 3, A) and the Gensini score with a correlation coefficient of -0.644 ($P<0.0001$, Fig. 3, B). The correlation analysis indicated a tight association between miR-30c-5p expression and ACS severity.

The risk factors assessment for the progression of ACS

The potential risk factors for the progression of ACS were determined by the multivariate logistic regression analysis and a variety of factors such as age, gender, BMI, T2DM, HBP, HLP, drinking, smoking, WBC, PLT, CK-MB, TC, TG, HDL-C, LDL-C, FBG, and miR-30c-5p were included in the analysis (Table 2). MiR-30c-5p was revealed to be a risk factor for ACS with the OR value of 0.081 (95% CI=0.029–0.226, P=0.000). A higher miR-30c-5p expression level demonstrated a lower possibility of the occurrence of ACS. Besides, the levels of HLP (OR: 4.068, 95% CI=1.208–13.700, P=0.024), PLT (OR: 2.649, 95% CI=1.057–6.638, P=0.038), CK-MB (OR: 3.477, 95% CI=1.342–9.010, P=0.010), and LDL-C (OR: 2.656, 95% CI=1.055–6.688, P=0.038) could also be the risk factors for ACS development and positively contributed to the progression of ACS.

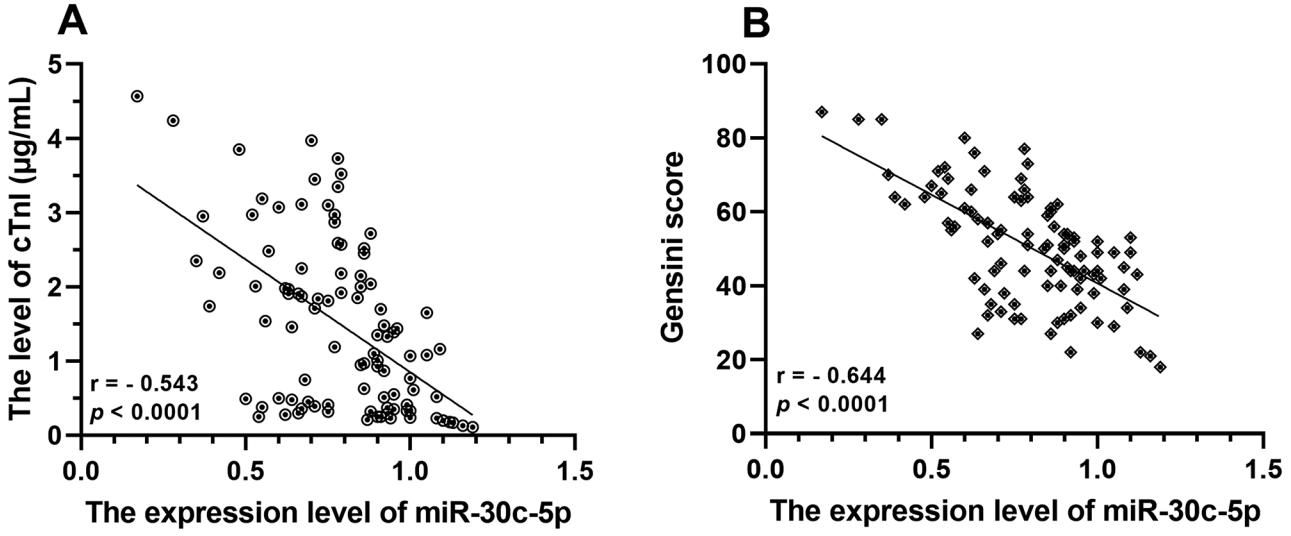

Fig. 3 The correlation between miR-30c-5p expression and the levels of cardiac troponin I (**A**) and Gensini score (**B**) in acute coronary syndrome

Table 2 Multivariate logistic regression analysis of risk factors for ACS

Factor	OR	95% CI	*P*-value
miR-30c-5p	**0.081**	**0.029–0.226**	**0.000***
Age	1.326	0.517–3.398	0.557
Gender	0.667	0.251–1.776	0.418
BMI	1.616	0.663–3.937	0.291
T2DM	3.117	0.997–9.742	0.051
HBP	3.047	0.765–12.141	0.114
HLP	**4.068**	**1.208–13.700**	**0.024***
Drink	1.953	0.690–5.531	0.207
Smoke	2.082	0.764–5.673	0.152
WBC	2.157	0.876–5.309	0.094
PLT	**2.649**	**1.057–6.638**	**0.038***
CK-MB	**3.477**	**1.342–9.010**	**0.010***
TC	1.307	0.534–3.195	0.558
TG	2.394	0.964–5.942	0.060
HDL-C	0.447	0.184–1.086	0.075
LDL-C	**2.656**	**1.055–6.688**	**0.038***
FBG	1.059	0.437–2.568	0.899

Note *$P<0.05$. BMI: body mass index; T2DM: type II diabetes mellitus; HBP: hypertension; HLP: hyperlipidemia; WBC: white blood cells; PLT: platelet; CK-MB: creatine kinase isoenzymes - MB; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FBG: fasting blood glucose

The association between miR-30c-5p expression and the prognosis of ACS

Based on the mean value of the miR-30c-5p expression, ACS subjects were classified into two groups: a high miR-30c-5p expression group ($n=48$) and a low miR-30c-5p expression group ($n=50$). The correlation between the expression level of miR-30c-5p and MACE occurrence in ACS subjects was shown in Table 3. The incidence of MACE in the low miR-30c-5p group was 50.00%, while that of the high miR-30c-5p group was 27.08%, indicating that miR-30c-5p expression levels were closely associated with the incidence of MACE in ACS ($P=0.020$). In a comparison of the high miR-30c-5p expression group, an obviously higher incidence of MACE was also confirmed in the low miR-30c-5p group by the K-M analysis ($P=0.013$, Fig. 4).

Table 3 The association between miR-30c-5p expression and MACE incidence in subjects with ACS

Variables	Low miR-30c-5p expression ($n=50$)	High miR-30c-5p expression ($n=48$)	*P*-value
Total MACE	**25 (50.00%)**	**13 (27.08%)**	**0.020***
Death	4 (8.00%)	2 (4.17%)	0.429
Angina	7 (14.00%)	4 (8.33%)	0.374
Revascularization	5 (10.00%)	3 (6.25%)	0.498
Reinfarction	3 (6.00%)	1 (2.08%)	0.327
Heart failure	6 (12.00%)	3 (6.25%)	0.325

Note *$P<0.05$. MACE: Major adverse cardiac events

MiR-30c-5p was revealed to be the independent prognostic factor for MACE occurrence with the HR value of 0.306 and 95% CI of 0.122 ~ 0.766, demonstrating that miR-30c-5p could significantly predict the occurrence of MACE in ACS ($P=0.011$, Table 4). Additionally, cTnI (HR: 2.995, 95% CI = 1.124–7.982, $P=0.028$), hs-CRP (HR: 2.229, 95% CI = 1.021–4.866, $P=0.044$), and Gensini score (HR: 2.587, 95% CI = 1.171–5.716, $P=0.019$) could also serve as independent prognostic factors for MACE Table 4. Based on the HR values, the expression level of miR-30c-5p was revealed to be negatively correlated with the occurrence of MACE. While higher levels of cTnI, hs-CRP, and higher scores of Gensini could predict a higher incidence of MACE in subjects with ACS.

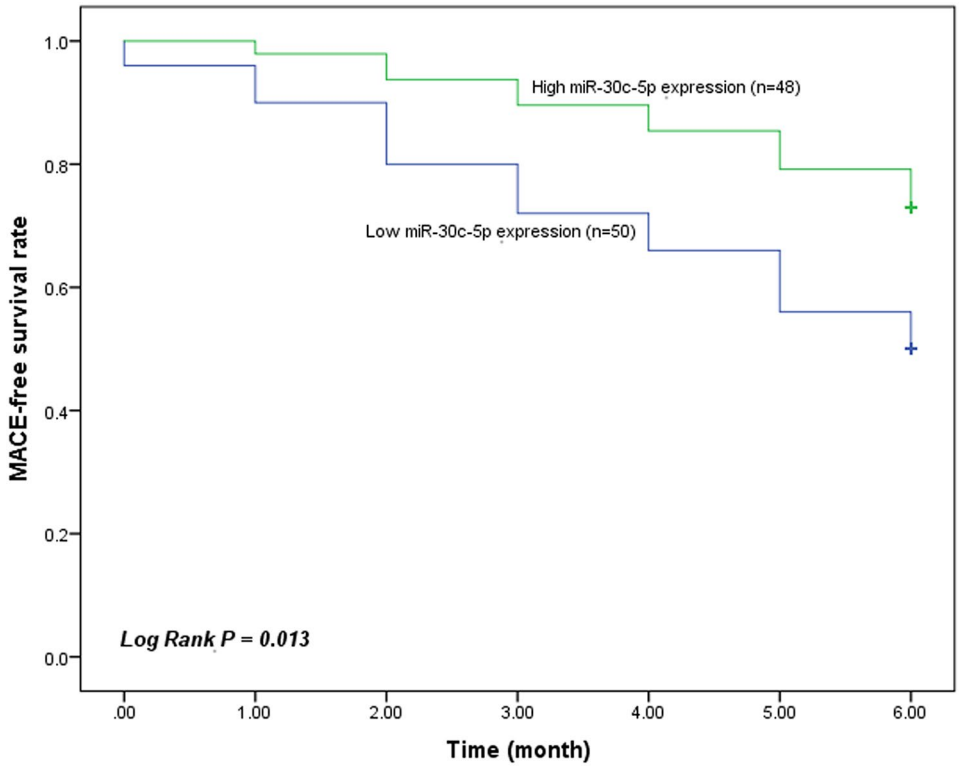

Fig. 4 The K-M curve about the association between miR-30c-5p expression and the incidence of MACE in acute coronary syndrome. A lower incidence of major adverse cardiovascular events was observed in the acute coronary syndrome subjects with higher miR-30c-5p expression

Discussion

Currently, the clinical diagnosis of ACS is primarily based on the patient's symptoms, electrocardiogram (ECGs), and the levels of cTnI and CK-MB [15]. However, atypical clinical symptoms of ACS may manifest in elderly and diabetic patients, while ECG may be influenced by left bundle branch block (LBBB) and chronic myocardial infarction, which can lead to misinterpretation of the results [16]. Besides, varying levels of cTnI and CK-MB are also observed in non-ACS patients such as severe infections, kidney failure, and congestive heart failure [17, 18]. In addition, some ACS patients after PCI will suffer from MACE, and effective monitoring could avoid the incidence of MACE in ACS patients [19]. Therefore, finding an accurate and convenient clinical biomarker is necessary for the diagnosis and prognosis of ACS. As a bridge of communication between cells and tissues, miRNAs are involved in plenty of pathological processes of ACS, including dyslipidemia, endothelial dysfunction, atherosclerotic plaque formation, myocardial ischemia caused by acute plaque rupture, and reperfusion injury [20]. According to the above information, miRNAs may play a significant role in diagnosing and treating ACS.

The role of miR-30c-5p dysregulation in atherosclerosis has been substantiated by evidence from multiple studies. For example, a downregulated miR-30c-5p expression was observed in human aortic endothelial cells (HAECs) induced by ox-LDL, while the overexpression of miR-30c-5p could inhibit inflammasome levels and pyroptosis in ox-LDL-induced HAECs [21]. Additionally, downregulated miR-30c-5p could promote the progression of early atherosclerosis by transmitting the pro-inflammatory and inhibiting the healing of endothelial [12]. As atherosclerosis was the pathological basis of ACS and severe atherosclerosis can be a causative factor for ACS, miR-30c-5p may also play a critical role in ACS. In our study, the downregulation of miR-30c-5p was identified in ACS patients, and its diagnostic value in ACS was confirmed according to the ROC curve, thus validating our initial hypothesis. AMI and UAP are two distinct types of ACS. In contrast to UAP, AMI is a more severe condition. Insufficient blood supply to the affected myocardium in AMI patients will result in myocardial necrosis, which can have a significant impact on their lives. Compared with UAP, the miR-30c-5p expression in subjects with AMI was lower and could also diagnose AMI from UAP in ACS patients. Additionally, miR-30c-5p, along with HLP, levels of PLT, CK-MB, and LDL-C, were also identified to be risk factors for the progression of ACS according to the multivariate logistic regression analysis. For patients with HLP, lipid abnormalities will promote the progression of atherosclerosis and lead to narrowing and blockage of coronary arteries, increasing the risk of myocardial infarction in ACS [22].

Table 4 The evaluation of independent prognostic factors for MACEs in ACS subjects by multivariate COX regression analysis

Indicators	HR	95% CI	*P*-value
miR-30c-5p	**0.306**	**0.122–0.766**	**0.011***
Age	1.222	0.545–2.740	0.626
Gender	0.626	0.279–1.404	0.256
BMI	1.351	0.591–3.088	0.476
T2DM	1.261	0.476–3.338	0.641
HBP	1.133	0.468–2.743	0.783
HLP	1.819	0.788–4.197	0.161
Drink	1.069	0.435–2.625	0.885
Smoke	1.013	0.401–2.555	0.979
WBC	1.078	0.468–2.480	0.861
PLT	1.764	0.760–4.095	0.186
CK-MB	1.789	0.793–4.035	0.161
TC	1.358	0.572–3.226	0.488
TG	1.140	0.518–2.512	0.744
HDL-C	0.675	0.305–1.494	0.332
LDL-C	1.363	0.638–2.912	0.424
FBG	1.687	0.740–3.846	0.213
cTnI	**2.995**	**1.124–7.982**	**0.028***
hs-CRP	**2.229**	**1.021–4.866**	**0.044***
GS	**2.587**	**1.171–5.716**	**0.019***

Note *$P<0.05$. BMI: body mass index; T2DM: type II 2 diabetes mellitus; HBP: hypertension; HLP: hyperlipidemia; WBC: white blood cells; PLT: platelet; CK-MB: creatine kinase isoenzymes - MB; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FBG: fasting blood glucose; cTnI: cardiac troponin I; hs-CRP: hypersensitive C-reactive protein; NT-proBNP: N-terminal B-type natriuretic peptide precursor; GS: Gensini score

The levels of PLT and CK-MB were also reported to be associated with ACS. Repeated PLT activation will contribute to the death risk of ACS by accumulating in the coronary arteries and thrombosing [23]. Thrombosis may result in the exacerbation of coronary artery stenosis or even complete occlusion among ACS patients, which can precipitate myocardial ischemia and hypoxia, as well as cardiomyocyte apoptosis. Apoptotic cardiomyocytes release CK-MB into the bloodstream, resulting in an elevation of CK-MB levels [24]. While compared with the CK-MB levels, the cTnI levels showed higher specificity in diagnosing ACS and could predict the progression of ACS and serve as a risk factor [25]. The Gensini score is one of the scoring systems for evaluating the severity of lesions in the coronary artery. The higher the Gensini score, the more serious the coronary artery lesions [26]. According to the correlation analysis, a negative relationship between miR-30c-5p expression and the levels of cTnI and Gensini score was revealed, indicating the close association between the miR-30c-5p levels and the severity of ACS. Given that the miR-30c-5p expression level in subjects with AMI was lower than that of subjects with UAP, the tight correlation between expression levels of miR-30c-5p and ACS severity was further confirmed.

Patients with AMI are at increased risk of MACE due to myocardial infarction caused by myocardial ischemic injury. Furthermore, AMI patients may also face the threat of post-operative ischemia-reperfusion injury resulting in MACE after surgical treatment. Thus, the occurrence of MACE is usually utilized to assess the safety and efficacy of clinical therapy for ACS and the prediction of MACE can enable ACS patients to receive further therapeutic intervention in time to avoid the occurrence of MACE [27, 28]. ACS subjects with lower miR-30c-5p expression showed a higher incidence of MACE, suggesting that low miR-30c-5p expression correlated with poor prognosis in ACS patients. Multivariate COX regression analysis was widely utilized in assessing the influence of different factors on the survival status of patients [29]. In this research, miR-30c-5p was identified as the independent prognostic factor for MACE in ACS.

Some limitations still existed in this study. First, the sample size was relatively small. Only 178 subjects involved in this study may not fully reflect the variation of the miR-30c-5p expression among the overall population. Second, the potential regulatory mechanism of miR-30c-5p in ACS was not fully explored. ACS progression typically involves inflammation and vascular endothelial injury in plaques. And miR-30c-5p was reported to suppress the inflammatory response and endothelial injury by regulating the expression of LDHA [30]. LDHA might also serve as the regulatory target of miR-30c-5p in ACS. However, this study only explored the trend of the expression levels of miR-30c-5p in all subjects and its predictive effect on ACS and MACE occurrence, the mechanism by which miR-30c-5p may regulate ACS at the molecular level has not been further investigated. In further research, more participants will be involved and the possible regulatory mechanism of miR-30c-5p/LDHA on ACS will be evaluated.

Conclusion

Serum miR-30c-5p expression was downregulated in ACS patients and closely correlated with ACS severity. The downregulated miR-30c-5p expression showed a diagnostic value on ACS and could predict the MACE occurrence in ACS. Moreover, miR-30c-5p was identified as the risk factor for ACS and an independent prognostic factor for MACE in ACS patients.

Acknowledgements

Not applicable.

Author contributions

Conceptualization, B.C., X.Z., R.F., H.L. and Y.W.; Data curation, B.C., X.Z., R.F. and Y.Z.; Formal analysis, R.F. and Y.Z.; Funding acquisition, H.L.; Investigation, R.F. and Y.Z.; Methodology, B.C., X.Z., R.F., H.L. and Y.W.; Project administration, H.L.; Resources, R.F. and Y.Z.; Software, R.F. and Y.Z.; Supervision, H.L.; Validation, R.F. and Y.Z.; Visualization, R.F.; Roles/Writing - original draft, B.C., X.Z. and R.F.; Writing - review & editing, H.L. and Y.W.

Funding
The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

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
The study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of The First People's Hospital of Xiaoshan District before the study began. The informed consent has been obtained from the participants involved.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 27 August 2024 / Accepted: 24 December 2024
Published online: 04 January 2025

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