**miR-941 as a promising biomarker for acute coronary syndrome**

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**Abstract**

**Background:** Circulating miRNAs can function as biomarkers for diagnosis, treatment, and prevention of diseases. However, it is unclear whether miRNAs can be used as biomarkers for acute coronary syndrome (ACS). To this end, we applied gene chip technology to analyze miRNA expression in patients with stable angina (SA), non-ST elevation ACS (NSTE-ACS), and ST-segment elevation myocardial infarction (STEMI).

**Methods:** We enrolled patients with chest pain who underwent diagnostic coronary angiography, including five patients each with SA, NSTE-ACS, or STEMI, and five controls without coronary artery disease (CAD) but with three or more risk factors. After microarray analysis, differential miRNA expression was confirmed by quantitative real-time reverse transcription polymerase chain reaction (qRT-PCR).

**Results:** Compared with those in patients with STEMI, differentially expressed microRNAs in controls and patients with SA or NSTE-ACS were involved in inflammation, protein phosphorylation, and cell adhesion. Pathway analysis showed that differentially expressed miRNAs were related to the mitogen-activated protein kinase signaling, calcium ion pathways, and cell adhesion pathways. Compared with their expression levels in patients with STEMI, miR-941, miR-363-3p, and miR-182-5p were significantly up-regulated (fold-change: 2.0 or more, \( P < 0.05 \)) in controls and patients with SA or NSTE-ACS. Further, qRT-PCR showed that plasma miR-941 level was elevated in patients with NSTE-ACS or STEMI as compared with that in patients without CAD (fold-change: 1.65 and 2.28, respectively; \( P < 0.05 \)). Additionally, miR-941 expression was significantly elevated in the STEMI group compared with that in the SA (\( P < 0.01 \)) and NSTE-ACS groups (\( P < 0.05 \)). Similarly, miR-941 expression was higher in patients with ACS (NSTE-ACS or STEMI) than in patients without ACS (without CAD or with SA; \( P < 0.01 \)). There were no significant differences in miR-182-5p and miR-363-3p expression. The areas under the receiver operating characteristic curves were 0.896, 0.808, and 0.781 for patients in the control, SA, and NSTE-ACS groups, respectively, compared with that for patients with STEMI; that for the ACS group compared with the non-ACS group was 0.734.

**Conclusion:** miR-941 expression was relatively higher in patients with ACS and STEMI. Thus, miR-941 may be a potential biomarker of ACS or STEMI.

**Keywords:** microRNA, Stable angina, Acute ST-segment elevation myocardial infarction, Acute coronary artery disease

**Background**

Acute coronary syndrome (ACS) is a major cause of death and disability [1]. Rapid antiplatelet therapy and revascularization could prevent myocardial ischemia and reduce the incidence of cardiovascular events [2]. Thus, the early diagnosis of non-ST elevation ACS (NSTE-ACS) and ST-segment elevation myocardial infarction (STEMI) is essential for improved prognoses. Currently, the clinical diagnosis of ACS relies on assessment of symptoms, ischemia changes in electrocardiogram (ECG), and changes in troponin [2]. However, in elderly individuals and patients with diabetes, typical symptoms are not always observed. Moreover, changes in ECG can be easily influenced by left bundle branch blockage and chronic myocardial infarction. To a certain extent, unstable angina pectoris (UA), non-STEMI (NSTEMI), and STEMI reflect the pathological progress of ACS. Therefore, identification of novel
Biomarkers may facilitate the early diagnosis of ACS, particularly in patients with atypical symptoms of ACS. MicroRNAs (miRNAs) are endogenous, small (22–24-nucleotide) noncoding RNA molecules that regulate the expression of mRNA by forming base pairing with the 3′-untranslated region (3′-UTR), subsequently triggering the degradation of mRNA or having negative effects on transcription [3]. miRNAs can regulate nearly 60% of coding genes to exert their biological functions [4, 5]. Recently, many studies have shown that miRNAs can regulate endothelial dysfunction, inflammation, cell autophagy, platelet activation, and aggregation [6–9]. Moreover, miRNA expression can affect the stability of atherosclerotic plaques [10]. miRNAs possess tissue-specific expression and can be secreted into blood or urine. miRNAs of circulatory system can be used as biomarkers for diagnosis, treatment, and prevention of diseases, such as coronary heart disease [11–14]. However, it is still unclear whether miRNAs can be used as biomarkers of ACS and further evaluate the severity of ACS [15].

Therefore, in this study, we applied gene chip technology to analyze the expression of miRNAs in patients with stable angina (SA), NSTE-ACS, and STEMI. We then performed quantitative real-time reverse transcription polymerase chain reaction (qRT-PCR) to determine whether miRNAs could be used as biomarker for the diagnosis of ACS.

**Methods**

**Patients and study design**

A total of 72 patients with chest pain who underwent diagnostic coronary angiography in Xiyuan Hospital, affiliated hospital of China Academy of Chinese Medical Sciences were enrolled from March 2015 to July 2015. The patients were divided into four groups as follows: 18 patients with STEMI, 18 patients NSTE-ACS, 20 patients with SA, and 16 patients without CAD. Patients in the control group did not have coronary stenosis as confirmed by coronary angiography, but had three or more risk factors for coronary heart disease (see schematic of the study in Fig. 1). Five cases were randomly selected from each group for analysis of gene expression profiles, using an Affymetrix GeneChip miRNA4.0. The differential expression of miRNAs between groups was analyzed according to the following criteria: fold-change (FC), ≥ 1.5 and P < 0.05. qRT-PCR was applied to verify the differential expression of miRNAs (FC, ≥ 2; P < 0.05). This study was registered in the Chinese Clinical Trial Registry (no. ChiCTR-IPR-15006336). The study was performed according to the guidelines of the Declaration of Helsinki and was approved by the Xiyuan Hospital Ethics Committee.

**Diagnostic criteria**

In this study, patients with coronary heart disease were classified as having SA or ACS, including STEMI, NSTE-ACS, and UA. Diagnostic criteria was refered to the 2014 ACC/AHA/AATS/PCNA/SCAI/STS Focused Update of the Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease [16], 2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes [2], and 2013 ACCF/AHA Guideline for the Management of ST-elevation Myocardial Infarction [17]. In addition, all patients presented stenosis (≥ 50% in at least one main coronary artery) as confirmed by coronary angiography [18].

**Inclusion and exclusion criteria**

The inclusion criteria were as follows: patients who met the diagnostic criteria, were 35–75 years old, and provided informed consent. The exclusion criteria were as follows: Patients with combined diseases, such as cardiomyopathy, valvular heart disease, severe arrhythmia, heart failure, and other accompanying diseases; patients encountered challenges with data collection, such as religious or language barriers; patients were pregnant or lactating and participating in other clinical studies.

**Blood collection and storage**

Venous blood samples were collected via antecubital venipuncture from each subject within 3–5 h of the onset of symptoms but before arteriography. Whole blood samples (2 mL) were collected directly into EDTA-containing tubes (BD, Franklin Lakes, NJ, USA), and three volumes of red blood cell lysis buffer (NH4CL2009; Haoyang, Tianjin, China) was added to obtain leukocytes, which were isolated within 2 h by centrifugation at 3000 rpm for 5 min at 4 °C to remove other blood elements. Next, 1 mL TRIzol (15596–026; Invitrogen Life Technologies) was...
added, and samples were then transferred to RNase/ DNase-free tubes and stored at –80 °C.

RNA isolation and preparation
After collection of all samples, total RNA in leukocytes was isolated using a miRvana RNA Isolation Kit (p/n AM1556; Applied Biosystems, Foster City, CA, USA) according to the manufacturer’s specifications. Samples were then subjected to on-column DNase I treatment with RNase-free DNase (#79254; Qiagen, Valencia, CA, USA). RNA quantity and quality were determined using a NanoDrop 2000 spectrophotometer (Thermo Scientific, USA) and an Agilent 2100 bioanalyzer. The RNA integrity was evaluated by agarose gel electrophoresis with ethidium bromide staining.

miRNA array analysis
Microarray analysis of gene expression was carried out using ELOSA QC Assays prior to array hybridization. Sample labeling, microarray hybridization, and washing were performed based on the manufacturer’s standard protocols. Briefly, total RNA was modified with poly A tails and then labeled with biotin. Next, the labeled RNAs were hybridized onto the microarray. Slides were washed and stained, and the arrays were scanned using an Affymetrix Scanner 3000 (Affymetrix).

miRNA microarray analysis was performed to determine differential expression of blood-borne miRNAs among (i) non-CAD individuals and patients with STEMI (n = 5), (ii) patients with SA and STEMI (n = 5), and (iii) patients with NSTE-ACS and STEMI. Bioinformatic determination of downstream predicted targets for candidate miRNAs was performed as described previously by Selbach et al. [19].

Reverse transcription quantitative real-time polymerase chain reaction (RT-qPCR) analysis
Quantification was performed through two-step reaction process: reverse transcription (RT) and qPCR. Each RT reaction consisted of 1 μg RNA, 4 μL miScript HiSpec Buffer, 2 μL Nucleics Mix, and 2 μL miScript Reverse Transcriptase Mix (Qiagen, Germany), in a total volume of 20 μL. Reactions were performed in a GeneAmp PCR System 9700 (Applied Biosystems, USA) for 60 min at 37 °C, followed by heat inactivation of the reverse transcriptase for 5 min at 95 °C. The 20-μL reaction mix was then diluted 5-fold in nuclease-free water and stored at –20 °C.

Real-time PCR was performed using a LightCycler 480II Real-time PCR Instrument (Roche, Switzerland) with 10 μL of the reaction mixture including 1 μL cDNA, 5 μL 2× LightCycler 480 SYBR Green I Master (Roche), 0.2 μL universal primers (Qiagen), 0.2 μL miRNA-specific primer, and 3.6 μL nuclease-free water. Reactions were incubated in a 384-well optical plate (Roche) at 95 °C for 10 min, followed by 40 cycles of 95 °C for 10 s and 60 °C for 30 s. Triplicates were averaged to calculate the expression value for each sample. At the end of the PCR cycling, melt curve analysis was performed to validate the specific generation of the expected PCR product. miRNA-specific primer sequences were designed in the laboratory and synthesized by Generay Biotech (Generay, PRC) based on the miRNA sequences obtained from the miRBase database (Release 20.0) as follows: hsa-miR-182-5p, UUUGG CAAUGGUAGAACUCACU; hsa-miR-363-3p, AAU UGCACGGUAUCCAUUGUA; and hsa-miR-941, CACCUGUGUGACCAUGUGC.

The expression levels of miRNAs were normalized to U6 and were calculated by the $2^{-\Delta\Delta Ct}$ method [20].

Statistical analysis
Affymetrix GeneChip Command Console software (version 4.0, Affymetrix) was used to analyze array images to obtain raw data, and RNA normalization was then carried out. Next, Genespring software (version 12.5, Agilent Technologies) was used for subsequent data analysis. Differentially expressed miRNAs were then identified through fold changes, and P-values were calculated using t-tests. The threshold set for up- and downregulated genes was a fold change of 1.5 or more and a P value of less than 0.05. Target genes of differentially expressed miRNAs were the intersection predicted with three databases (Targetscan, PITA, and microRNAorg). Gene ontology (GO) analysis and KEGG analysis were applied to determine the roles of these target genes. Hierarchical clustering was performed to show distinguishable miRNA expression patterns among samples.

Paired and unpaired Student's t tests were performed to compare data as appropriate. Values are expressed as means ± standard deviations (SDs). P values of less than 0.05 (two-sided) were considered significant.

Results
Patient clinicopathological information
Seventy-two patients (18 patients with STEMI, 18 patients with NSTE-ACS, 20 patients with SA, and 16 patients without CAD) were enrolled in this study. The clinicopathological characteristics of the patients are presented in Tables 1 and 2. There were no significant differences in clinical features among groups ($P > 0.05$).

miRNA array analysis
The differential expression of miRNAs among the patient groups was determined by gene chip analysis. The results showed that there exist 13 differentially expressed miRNAs in patients with STEMI comparing with those in patients without CAD and patients with SA and NSTE-ACS. After that, we chose miR-941, miR-363-3p, and miR-182-5p ($FC_{\geq 2.0}$; $P < 0.05$) for further analysis by qRT-PCR (Table 3).
ACEI, calcium channel blocker, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker

Table 1 Baseline clinical characteristics of different patient groups used in microarray analysis

| Variable                  | CAD (n = 15) | Without CAD (n = 5) |
|---------------------------|--------------|---------------------|
|                           | SA (n = 5)   | NSTE-ACS (n = 5)    | STEMI (n = 5) |
| Age (years, mean ± SD)    | 55.8 ± 4.15  | 57.4 ± 11.19        | 52.8 ± 10.56  |
| Sex (male, n)             | 5            | 5                   | 5             |
| Risk factors (n)          |              |                     |               |
| Hypertension              | 4            | 4                   | 2             |
| Dyslipidemia              | 5            | 3                   | 4             |
| Active smoker             | 4            | 3                   | 5             |
| Medications (n)           |              |                     |               |
| Antiplatelet agents       | 5            | 5                   | 5             |
| ß-Blockers                | 4            | 3                   | 3             |
| CCB                       | 2            | 1                   | 1             |
| ACEI/ARB                  | 4            | 4                   | 4             |
| Statins                   | 5            | 5                   | 5             |

Abbreviations: SA: stable angina, NSTE-ACS: non-ST elevation acute coronary syndrome, STEMI: ST elevation myocardial infarction, DM: diabetes mellitus, CCB: calcium channel blocker, ACEI: angiotensin-converting enzyme inhibitor, ARB: angiotensin receptor blocker

Gene ontology (GO) analysis

Differentially expressed miRNAs in patients without CAD and with SA or NSTE-ACS (compared with that in patients with STEMI) were found to be involved in inflammation, protein phosphorylation, RNA polymerase II-dependent transcription, cell adhesion, and other biological processes. Among these, inflammation, cell adhesion, T-cell proliferation, calcium transfer, and apoptosis were closely related to atherosclerosis (Fig. 2).

Pathway analysis

The KEGG database was used to analyze target genes of differentially expressed miRNAs. Differentially expressed miRNAs in control and in patients with SA or NSTE-ACS compared with that in patients with STEMI were found to regulate biological processes such as mitogen-activated protein kinase (MAPK) signaling, tumorigenesis, and calcium ion signaling. Among the identified cell signaling pathways, we identified the following pathways involved in the pathological process of atherosclerosis: adhesion molecules, ErbB signaling, metabolism, Wnt signaling, insulin signaling, apoptosis, vascular endothelial growth factor signaling, and cell factor receptor interactions (Fig. 3).

miRNA-pathway network analysis showed that miR-941 can participate in regulation of T-cell receptor signaling, insulin signaling, and MAPK signaling. Additionally, miR-182-5p was related to vascular smooth muscle cell constriction and mammalian target of rapamycin (mTOR) signaling. miR-363-3p was involved in Toll-like receptor signaling and actin cytoskeleton regulation. Bioinformatics functional predictions showed that the differential expressed miRNAs could be related to the pathological process of cardiovascular disease (Fig. 4).

qRT-PCR

Next, we performed qRT-PCR to verify the different expression of candidate gene like, miR-941, miR-182-5p, and miR-363-3p. The results showed that miR-941 expression has no significant difference between the control patients (without CAD) and SA group. However, comparing with control patients, miR-941 expression was significantly increased by 1.64- and 2.28-fold in patients with NSTE-ACS and STEMI, respectively, (P < 0.05; Fig. 5a). There were no significant differences in miR-182-5p and miR-363-3p among groups (P > 0.05; Fig. 5b and c). Additionally, the expression of miR-941 was increased by 1.66-fold in patients with STEMI compared with that in patients with SA (P < 0.001; Fig. 6a-1) and by 1.52-fold in patients with STEMI compared with that in patients with NSTE-ACS (P < 0.05; Fig. 6a-2). There were no significant differences in miR-182-5p and miR-363-3p (P > 0.05; Fig. 6b and c).

Since there were no significant differences in miR-941 expression between patients without CAD and patients with SA, we combined the two groups into the non-ACS group. Compared with that in the non-ACS group, the expression of miR-941 was upregulated in the ACS group (FC: 1.62; P < 0.01; Fig. 7). NSTE-ACS and other biological processes.
STEMI can reflect the degree of disease progression, and miR-941 was significantly upregulated in patients with STEMI compared with that in patients in the non-ACS group (FC: 1.52; \(P < 0.05\); Fig. 6a-2). The differential expression of miR-941 in the two groups showed that the expression of miR-941 was associated with the severity of ACS.

### Receiver operating characteristic (ROC) curve analysis

Next, we performed ROC curve analysis to test the reliability of miR-941 as a diagnostic biomarker of STEMI and ACS. Comparing with patients with STEMI, areas under the ROC curves were 0.896, 0.808, and 0.781 for patients in the control, SA, and NSTE-ACS groups, respectively; Comparing with patients in ACS group,

### Table 3 Differentially expressed miRNAs in patients with ACS versus patients without CAD and patients with SA or NSTE-ACS in microarray analysis

| miRNAs       | STEMI versus without CAD | STEMI versus SA | STEMI versus NSTE-ACS |
|--------------|--------------------------|----------------|-----------------------|
|              | Fold change  | P value | Regulation | Fold change  | P value | Regulation | Fold change  | P value | Regulation |
| miR-941      | 5.305        | 0.007   | Up         | 4.544        | 0.003   | Up         | 5.032        | 0.002   | Up         |
| miR-182-5p   | 2.331        | 0.013   | Down       | 2.005        | 0.042   | Down       | 2.121        | 0.024   | Up         |
| miR-363-3p   | 2.012        | 0.007   | Down       | 2.016        | 0.018   | Down       | 2.071        | 0.048   | Up         |
| hsa-miR-941-1| 1.895        | 0.036   | Up         | 2.051        | 0.001   | Up         | 2.008        | 0.001   | Up         |
| hsa-miR-941-2| 1.895        | 0.036   | Up         | 2.051        | 0.001   | Up         | 2.008        | 0.001   | Up         |
| hsa-miR-941-3| 1.895        | 0.036   | Up         | 2.051        | 0.001   | Up         | 2.008        | 0.001   | Up         |
| hsa-miR-941-4| 1.895        | 0.036   | Up         | 2.051        | 0.001   | Up         | 2.008        | 0.001   | Up         |
| hsa-miR-6798-5p | 2.049 | 0.015 | Up | 1.866 | 0.019 | Up | 2.041 | 4.32E-04 | Up |
| hsa-miR-4419a | 1.737 | 0.013 | Up | 1.717 | 0.006 | Up | 1.851 | 9.32E-05 | Up |
| hsa-miR-296-3p | 1.811 | 0.031 | Up | 2.209 | 0.012 | Up | 1.726 | 0.109 | Up |
| hsa-miR-1227-5p | 1.549 | 0.013 | Up | 1.629 | 0.039 | Up | 1.653 | 0.147 | Up |
| hsa-miR-4656 | 1.908 | 0.005 | Up | 1.617 | 0.025 | Up | 1.232 | 0.459 | Up |
| hsa-miR-3064-3p | 1.765 | 0.037 | Down | 1.529 | 0.001 | Down | 1.033 | 0.738 | Down |

**Abbreviations:** SA stable angina, NSTE-ACS non-ST segment elevation acute coronary syndrome, STEMI ST segment elevation acute myocardial infarction

**Fig. 2** Gene ontology (GO) analysis
ROC curves of non-ACS group was 0.734 (Fig. 8). Thus, miR-941 may act as a reliable biomarker of ACS, particularly STEMI. The area under the curve (AUC), 95% confidence intervals (CIs), and $p$ values are summarized in Table 4.

**Discussion**

Aberrant miRNA expression has been involved with a number of human diseases, including cardiovascular diseases [11, 21–23]. ACS has become a major public health problem owing to its high mortality and
morbidity [24–26]. Thus, there is an urgent need to identify new diagnostic and therapeutic biomarkers of ACS; miRNAs may have such applications. MiRNAs are involved in endothelial dysfunction, inflammation, apoptosis, angiogenesis, atherosclerosis, and other pathological processes involved in cardiovascular diseases [6, 27, 28], and miRNAs of circulatory system may be potential biomarkers of these diseases [7, 29]. miR-135a, miR-31, miR-378, and miR-147 are biological markers of stable coronary heart disease [30]; miR-1, miR-126, and miR-133a have potential value in the diagnosis of UA [31]; and miR-208b, miR-499, and miR-1 play a key role in the diagnosis, progression, and prognosis of acute myocardial infarction (AMI) [15, 32–34]. However, it is unclear whether miRNAs are differentially expressed with changes in the severity of coronary heart disease, including coronary stenosis and myocardial damage. Our findings suggested that miR-363-3p, miR-941, and miR-182-5p were differentially expressed among groups of patients with various types and degrees of coronary heart disease. Additionally, GO and KEGG pathway analysis showed that the differentially expressed miRNAs were involved in inflammatory responses, immune responses, MAPK signal, calcium pathway, ErbB signaling, and other cellular processes. In particular, MAPK signaling and immune responses are involved in the pathogenesis of atherosclerosis and affect the stability of plaques and the formation of blood clots. Furthermore, qRT-PCR analysis verified that miR-941 was differentially expressed in plasma from patients with CADs (SA, NSTE-ACS, and STEMI) compared with that in patients without CAD. Abbreviations: CAD: coronary artery disease, SA: stable angina, NSTE-ACS: non-ST elevation acute coronary syndromes, STEMI: ST elevation myocardial infarction. *P < 0.05, ΔP < 0.001

Fig. 5 Expression profiles of candidate miRNAs in patients with and without CAD. The three candidate miRNAs were evaluated with qRT-PCR using 72 samples, including 16 non-CAD, 20 SA, 18 NSTE-ACS, and 18 STEMI samples. miR-941 was significantly upregulated in the SA, NSTE-ACS, and STEMI groups compared with that in non-CAD patients (a). miR-182-5p (b) and miR-363-3p (c) were not significantly different in patients with CAD (SA, NSTE-ACS, and STEMI) compared with that in patients without CAD. Abbreviations: CAD: coronary artery disease, SA: stable angina, NSTE-ACS: non-ST elevation acute coronary syndromes, STEMI: ST elevation myocardial infarction.
biomarker of ACS, particularly for STEMI, and could predict the severity and progression of coronary heart disease.

Recent bioinformatics analyses have shown that miR-941 is involved in Wnt signaling, transforming growth factor (TGF)-β signaling, and insulin signaling [35, 36]. However, no research has been reported the role of miR-941 in atherosclerosis and coronary heart disease.

In our study, we found that miR-941 may be associated with metabolism, inflammation, cell proliferation, and other biological processes through regulation of components involved in insulin signaling, MAPK signaling, T-cell receptor signaling, and other related pathways. However, we were not able to confirm the direct relationship between miR-941 and the pathogenesis of atherosclerosis. In vitro and in vivo experiments are needed to clarify the biological function of miR-941 in the pathophysiology of atherosclerosis and to determine

**Fig. 6** Expression profiles of candidate miRNAs in patients with SA, NSTE-ACS, and STEMI. The three candidate miRNAs were evaluated by qRT-PCR using 56 samples (20 cases of SA, 18 cases of NSTE-ACS, and 18 cases of STEMI). (a) miR-941, (b) miR-182-5p, and (c) miR-363-3p are shown. Abbreviations: CAD, coronary artery disease; SA, stable angina; NSTE-ACS, non-ST elevation acute coronary syndrome; STEMI, ST elevation myocardial infarction.

*P < 0.05, **P < 0.001

**Fig. 7** Expression profiles of miR-941 in patients with and without ACS. miR-941 expression was evaluated by qRT-PCR using 72 samples (36 patients without ACS and 36 patients with ACS). Abbreviations: ACS, acute coronary syndrome. ΔP < 0.01
whether miR-941 is involved in pathological processes of inflammation, immunity, metabolism, and platelet activation. Although we found that miR-941 was differentially expressed between ACS and non-ACS groups, additional studies are needed to establish a rapid, inexpensive method for miRNA analysis. Additionally, greater sample sizes are needed to further confirm the potential applications of this miRNA as a promising diagnostic tool for diagnosis of ACS.

Conclusions
MiR-941 was relatively higher in patients with ACS and STEMI, and could predict the severity and progression of coronary heart disease. Thus, miR-941 may be a potential biomarker of ACS or STEMI.

Additional files

**Additional file 1**: The mass detection report of samples. (DOCX 136 kb)
**Additional file 1**: Baseline Table 1. Original data of Baseline clinical characteristics of different groups used in microarray analysis. (XLSX 10 kb)
Additional file 3: Baseline Table 2: Original data of Baseline clinical characteristics of different groups used in qRT-PCR analysis. (XLSX 11 kb)

Additional file 4: miRNA-gene-network and miRNA-targets-relation. (XLSX 382 kb)

Additional file 5: Microarray pathway network Pathway-miRNA-relation and microarray pathway network. The red rectangles are miRNAs, the purple lines are pathways, and the green lines represented the regulatory connections between miRNAs and pathways. (XLSX 137 kb)

Additional file 6: Original data of Table 3: Differentially expressed miRNAs in microarray analysis. (XLSX 19 kb)

Additional file 7: Original data of Fig. 5a: MiR-941 was significantly upregulated in the SA, NSTE-ACS, and STEMI groups compared with that in non-CAD patients. (XLSX 14 kb)

Additional file 8: Original data of Fig. 5b: MiR-182-5p were not significantly different in patients with CAD (SA, NSTE-ACS, and STEMI) compared with that in patients without CAD. (XLSX 17 kb)

Additional file 9: Original data of Fig. 5c: MiR-363-3p were not significantly different in patients with CAD (SA, NSTE-ACS, and STEMI) compared with that in patients without CAD. (XLSX 17 kb)

Additional file 10: Original data of Fig. 6a-1: MiR-941 Expression profiles of candidate miRNAs in patients with SA, NSTE-ACS, and STEMI. The three candidate miRNAs were evaluated by qRT-PCR using 56 samples. (XLSX 13 kb)

Additional file 11: Original data of Fig. 6a-2: MiR-941 Expression profiles of candidate miRNAs in patients with SA, NSTE-ACS, and STEMI. The three candidate miRNAs were evaluated by qRT-PCR using 56 samples. (XLSX 13 kb)

Additional file 12: Original data of Fig. 6b: MiR-182-5p Expression profiles of candidate miRNAs in patients with SA, NSTE-ACS, and STEMI. The three candidate miRNAs were evaluated by qRT-PCR using 56 samples. (XLSX 15 kb)

Additional file 13: Original data of Fig. 6c: MiR-363-3p Expression profiles of candidate miRNAs in patients with SA, NSTE-ACS, and STEMI. The three candidate miRNAs were evaluated by qRT-PCR using 56 samples. (XLSX 15 kb)

Additional file 14: Original data of Fig. 7: Expression profiles of miR-941 in patients with and without ACS. (XLSX 15 kb)

Additional file 15: Table 4-ROC curve. Original data of ROC curve analysis of miR-941 expression in patients with ACS and STEMI. (XLSX 12 kb)

Abbreviations

3’UTR: 3′-untranslated region; ACS: Acute coronary syndrome; AMI: Acute myocardial infarction; AUC: Area under the curve; CI: Confidence interval; ECG: Electrocardiogram; FC: Fold-change; GO: Gene ontology; MAPK: Mitogen-activated protein kinase; miRNA: MicroRNA; MTOR: Mammalian-target of rapamycin; NSTE-ACS: Non-ST elevation ACS; qRT-PCR: Quantitative real-time reverse transcription polymerase chain reaction; ROC: Receiver operating characteristic; SA: Stable angina; STEMI: ST-segment elevation myocardial infarction; TGF: Transforming growth factor; UA: Unstable angina pectoris

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Availability of data and materials

All data from this study can be found in the Supplementary Material (Additional files 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 and 15).

Authors’ contributions

RB and QY were responsible for this manuscript and data analysis; these authors contributed equally to this manuscript. RX was responsible for data collection and follow-up. LL and DS modified the paper and gave constructive suggestions. KC made substantial contributions to conception and design. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Xiyuan Hospital Ethics Committee (approval no. 11: 2015SL-15-2), and all study participants provided written informed consent.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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