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Original Article

Identification of miRNA profile in the peripheral blood and clinical significance of miR-355 and miR-2911 expression in children with Kawasaki disease

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Abstract: Objective: To identify the abnormal expression profile of miRNA in peripheral blood of children with Kawasaki disease (KD) and explore its diagnostic value for Kawasaki disease. Methods: From January 2020 to June 2021, 62 children with KD (KD group) and 158 children with febrile disease (Con group) were selected as subjects. Peripheral blood was collected before treatment, and differentially expressed miRNAs in peripheral blood were identified by next generation sequencing, and the identified targets were verified by RT-PCR. The diagnostic value of miRNAs in KD was analyzed by ROC curves and linear SVM model. Results: Compared to Con group, a total of 163 differentially expressed miRNAs were detected in peripheral blood of children in the KD group, including 126 up-regulated miRNAs and 37 down-regulated miRNAs. Hierarchical clustering showed that miRNA profiles of children in the KD group and Con group were significantly different, among which 3 miRNAs wereup-regulated and 3 miRNAs were down-regulated ($P<0.05$). The results of miRanda and TargetScanS software showed that a total of 17159 target genes were predicted. GO function and KEGG signal pathway enrichment analysis showed that target genes were involved in a wide range of biological functions; ROC curve results showed that the sensitivity of miR-355 and miR-2911 in diagnosing KD were 73.8% and 71.2%, the specificity was 72.4% and 73.9%, and the AUC was 0.793 and 0.757, respectively. The AUC for combined detection of miR-355 and miR-2911 was increased to 0.806. A linear SVM model further verified the diagnostic value of joint detection of miR-355 and miR-2911. Conclusion: Expression levels of miR-355 and miR-2911 were significantly up-regulated in peripheral blood of children with Kawasaki disease. miR-355 and miR-2911 could serve as biomarkers for diagnosis of Kawasaki disease.

Keywords: Kawasaki disease, microRNAs, diagnosis, febrile disease, children

Introduction

Kawasaki disease (KD) is a cutaneous mucosal lymph node syndrome first reported by Japanese scholar Tomisaku Kawasaki [1]. The main clinical manifestations are acute fever, rash, mucosal vasculitis, hepatosplenic and lymph node enlargement. KD is an immune-mediated, self-limited acute systemic vasculitis syndrome commonly occurring in children under 5 years old of age and infants. KD mainly invades medium and small arteries throughout the body, and its serious complications are acute coronary syndrome, myocardial infarction, and coronary aneurysm, which has become the primary cause of secondary heart disease in children in China [2]. Early diagnosis and treatment of KD is of great significance to reduce the occurrence of coronary artery damage. KD is now the most common cause of acquired heart disease in children in both developed and developing countries [3]. KD mostly consists of complete Kawasaki disease (CKD), while incomplete Kawasaki disease (IKD) accounts for about 13%-30%. Due to atypical symptoms and signs of IKD, sometimes fever is the only main manifestation of IKD, although some inflammatory related indicators may be elevated, and the anti-infection effect is not ideal [4]. It is often difficult to make a clear diagnosis after a series of auxiliary examinations for “fever check”, which can easily delay the proper treatment of disease. The pathogenesis of IKD is related to immune disorders of the body [5]. Systemic

small vasculitis has been found in early stages of the disease. Abnormal changes are often observed through the detection of cytokines and related inflammatory indicators, especially tumor necrosis factor-α and the interleukin family, which have been widely studied, but none of them has specificity [6]. The etiology of KD is not clear at present, but there are several hypotheses such as infection, environmental pollution, and allergy. Early diagnosis and early intervention are the keys to KD treatment, but a "gold standard" for KD diagnosis is still lacking. However, the current diagnosis of KD mainly relies on clinical symptoms and lacks specific laboratory indicators. Therefore, finding biomarkers with high specificity for early diagnosis of KD is attracting attention.

MicroRNAs (miRNAs) are a class of endogenously expressed non-coding RNAs with 18-23 nucleotide sequences, widely existing in eukaryotic cell cytoplasm. Recent studies have found that mature miRNAs can dissociate from cells and exist stably in circulating blood. This has shown value in the early diagnosis and prognosis of various tumors and non-tumor diseases. Moreover, using plasma as test samples has the advantages of convenient sampling, with timely non-invasive and periodic continuous sampling [7]. These advantages make plasma circulating miRNAs possible new biomarkers for the diagnosis, treatment, and prognosis evaluation of KD [8]. In this study, the differential expression profile of circulating miRNAs in plasma of children with KD was detected to determine the role of plasma-specific circulating miRNAs in the pathogenesis of KD and to search for new biomarkers for the early diagnosis of KD.

Materials and methods

Research subjects

The study was approved by the institutional ethical committee of Jinan Maternity and Child Care Hospital Affiliated to Shandong First Medical University (Approval No. 2022-054). The guardians of patients signed informed consent forms. Children admitted to our hospital from January 2020 to June 2021 with fever as the chief complaint were selected as the research subjects. The patients diagnosed with KD were assigned to the Kawasaki disease group (n=62), and those with other febrile diseases, including tonsillitis, EPstein-Barr virus infection, conjunctival pharyngeal fever and sepsis, were in the fever control group (n=158).

The inclusion criteria of children with Kawasaki disease [9, 10]: ① Children with fever for more than 5 days and ineffective antibiotic treatment that was accompanied by four of the following five conditions: bilateral bulbar conjunctival hyperemia; lips, mouth chapping, diffuse congestion, waxberry tongue; Cervical lymph node enlargement; skin erythema and rash; flushing and swelling palmar and plantar and membranous desquamation of finger in convalescence. ② Patients who were not treated with large doses of gamma globulin, hormone, aspirin and other drugs for Kawasaki disease, and the course of disease was 5-9 days. ③ The children whose guardians signed the informed consent.

Exclusion criteria: ① Children who have started the treatment of Kawasaki disease; ② Patients with allergic purpura and other immune diseases; ③ Patients with incomplete clinical data.

In the Kawasaki disease group, there were 125 boys with an average age of (2.01±1.03) years old and 56 girls with an average age of (2.11±1.16) years old.

Diagnostic criteria for CKD and IKD

Diagnostic criteria of CKD: according to the diagnostic criteria of the American College of Cardiology, those who have sustained fever for more than 5 days (ineffective application of antibiotics) and have 4 or more of the following five clinical manifestations can be diagnosed after excluding other diseases: ① Limb changes: erythema on the palms and soles of hands and feet in the acute stage, hard edema of hands and feet, and membranous peeling at the ends of fingers and toes in the recovery stage; ② Bilateral conjunctival membrane congestion; ③ Pleomorphic rash; ④ Cervical lymph node enlargement that was more commonly unilateral; ⑤ Diffuse bleeding of oral mucosa, hyperemia and chapped lips, prominent tongue papilla, strawberry like; CKD can be also diagnosed if there are fewer than 4 items but cardiac involvement. IKD diagnostic criteria: according to the diagnostic criteria of the American College of Cardiology, IKD can be diagnosed only if fever ≥5 days, 2~3 character-

Table 1. Primer sequences

Gene	positive-sense strand	antisense strand
miR-355	5'-ATGACAGCTGACCACTGAG-3'	5'-ATTTGTTGCCCAGGAAAGTG-3'
miR-2911	5'-TTGGTTTCTGCCCTAGTGAGAGA-3'	5'-AAAGATGAACGGGAACACACAGG-3'
miRNA-100a	5'-TGTCGATGCAGCAAACCTCA-3'	5'-GACTTCTACAACGATCCCCTC-3'
miRNA-1	5'-CCTCGCCTTTGCCGATCC-3'	5'-GGATC TTCATGAGGTAGTCAGTC-3'
miRNA-200b	5'-GTCGTACCACAGGCATTG-3'	5'-GCAATGCCTGGGTACATGGTGG-3'
miRNA-145	5'-GCGGG CGCTGGAGGAGAA-3'	5'-GGATCTTCATGAGGTAGTCAGTC-3'
U6	5'-CTCGCTTCGGCAGCACA-3'	5'-AACGCTTCACGAATTTGCGT-3'

istics of KD symptoms, C-reactive protein >30 mg/L and 3 of the following items: ① Albumin ≤30 g/L; ② Abnormal liver function; ③ Anemia; ④ More than 7 days after onset, increased platelets and platelets >450 × 10^9; ⑤ Urine routine examination: leukocytes >10/HP field. Coronary artery damage: ① Coronary artery diameter: less than 2.5 mm from 6 months to 3 years old, and more than 3.0 mm from 3 to 9 years old; ② Coronary intimal echo enhancement.

Treatment of children

All children were prescribed aspirin effervescent tablets, 50 mg/kg, once a day for three times. After the fever subsided, it was reduced to 3~5 mg/kg, once a day for three times according to the patient's condition. Intravenous infusion of gamma globulin (Shenzhen Weiguang Biological Products Co., Ltd, batch No. 140822) 1.0 g/kg, once a day, continuous intravenous infusion for 8~12 h, and another shock treatment within 8~12 h, continuous application for 2 d.

Blood sample collection and sequencing analysis

The 62 samples collected were the peripheral blood of patients with KD at initial diagnosis, and the peripheral blood of 158 children with other febrile diseases treated in our hospital was collected at the same time. Blood was stored in an anticoagulant tube containing EDTA at -80°C for subsequent tests. The total RNA in peripheral blood was extracted with Trizol reagent Invitrogen kit, and the total RNA in peripheral blood was inspected. The sample concentration ≥1 ng/UL and the total sample amount ≥10 ng was needed to meet the requirements. Subsequently, a small RNA library was constructed using illuminatruseq small RNA kit. The Illumina Hiseq4000 high-throughput sequencer was used for sequencing, and the final concentration of the on-board sample was 10 pmol/L. Various miRNA were identified, and their expression amounts were obtained for differential expression analysis, sample specific expression miRNA analysis and PCR analysis.

Target gene prediction and functional analysis of miRNAs

MiRanda and TargetScanS software were used to jointly predict the results as candidate target genes of miRNA. The GO function and KEGG signal pathway enrichment of the predicted target genes were analyzed by software Goatools (https://github.com/tanghaibao/GOatools) and KOBAS (http://kobas.cbi.pku.edu.cn/kobas3/), respectively. The method was Fisher's exact test. P≤0.05 was considered a significant target gene.

RT-PCR detection

Total RNA was extracted from peripheral blood using RNA Isolation Kit according to the manufacturer's instructions, and U6 was used as an endogenous control. According to the instructions of the reverse transcription kit, 500 ng RNA template was reverse transcribed with 20 μl reaction system to obtain cDNA. Reverse transcription conditions: 37°C 15 min, 85°C 5 s. Phusion reaction system (Thermo Science) and SYBR premix ex Taq ™II (Takara) were used for quantitative RT-PCR. The reaction conditions were as follows: pre denaturation 5 min at 95°C, denaturation 28 s at 95°C, annealing 65 s at 60°C, extension 1 min at 68°C, with a total of 40 cycles. The primer sequences are shown in **Table 1**. PCR amplification was conducted. The Ct values of miRNAs were calculated using ABI 7300 System software. The relative expression levels of miRNAs were calculated using $2^{-\Delta\Delta Ct}$ method.

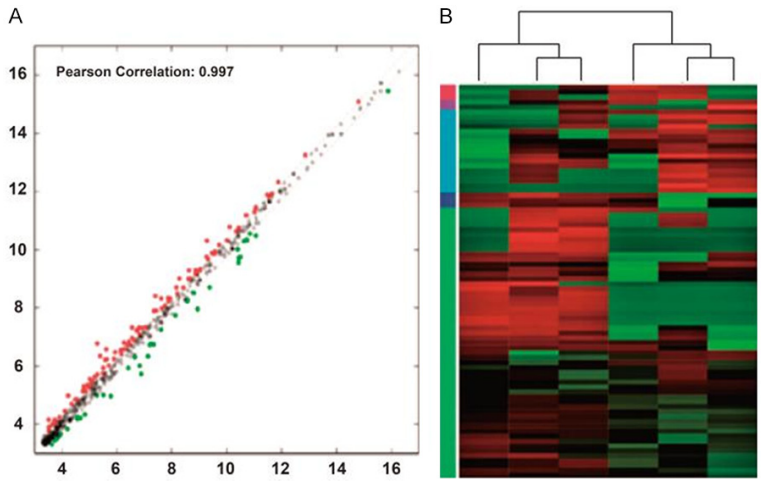

Figure 1. Sequencing analysis of miRNA in peripheral blood of children with Kawasaki disease. A: Differentially expressed miRNAs; B: Hierarchical clustering results.

Statistical methods

SPSS 20.0 software was used for statistical analysis. The measured data were expressed as mean ± standard deviation (SD) and the counted data were expressed as percentages. Independent sample T test was applied to analyze the differences in measured data between two groups. Chi-square test was used to analyze differences in counted data between two groups. The significant variables were analyzed by multivariable analysis as independent predictors for the diagnosis of KD. ROC curve and AUC (95% CI) were used to evaluate the diagnostic efficacy of miRNA-355 and miRNA-2911 for KD.

Linear support vector machine (SVM) machine learning analysis model was applied to rank the importance of the detected miRNAs for distinguishing children with Kawasaki disease from those in the febrile control group. The top two miRNAs were used as blood biomarkers and to calculate the predicted value. The prediction model was established which was validated in other samples. $P<0.05$ was considered a significant difference.

Results

Differential expression of miRNAs in peripheral blood

As shown in **Figure 1**, compared to the Con group, 163 differentially expressed miRNAs were detected in the peripheral blood of children in KD group, of which 126 were up-regulated and 37 were down-regulated. The miRNA profiles of children in KD group and Con group were significantly different (more than two times), in which 3 miRNAs were significantly up-regulated and 3 miRNAs were down-regulated ($P<0.05$).

Verification of differential expression of miRNAs

RT-PCR was used to verify the differentially expressed miRNAs that were highly expressed in peripheral blood. Six miRNAs including miRNA-355, miRNA-2911, miRNA-100a, miRNA-1, miRNA-200b and miRNA-145, were selected for RT-PCR verification in the peripheral blood of children in the two groups, as shown in **Figure 2**. RT-PCR results showed that compared to the Con group, the expression levels of miRNA-355, miRNA-2911, and miRNA-100a in peripheral blood of KD children were significantly up-regulated ($P<0.05$), and the expression level of miRNA-1 was significantly down-regulated ($P<0.05$), but there was no significant difference in the expression levels of miRNA-200b and miRNA-145 ($P>0.05$). The RT-PCR results were consistent with next generation sequencing results.

Bioinformatics analysis of differentially expressed miRNAs

Target genes of known differentially expressed miRNAs were predicted by miRanda and TargetScanS software, and a total of 17159 target genes were predicted. GO analysis of target differentially expressed miRNAs shows that the target genes participate in a wide range of biological functions, and the enriched biological functions include ionotropic glutamate receiver signaling pathway, regulation of amino acid transport Lipopolysaccharide mediated signaling pathway and apoptotic process involved development, as shown in **Figure 3A**. Through further pathway analysis, it was found that the signal pathways with relatively significant enrichment included chemokine signaling

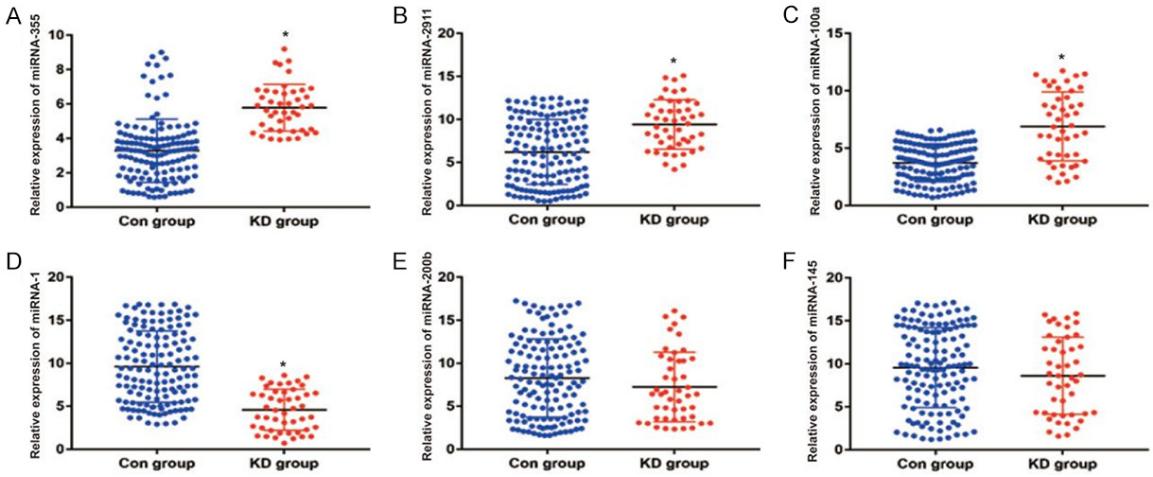

Figure 2. The expression of miRNAs in peripheral blood of two groups detected by PCR. A: miRNA-355 expression; B: miRNA-2911 expression; C: miRNA-100a expression; D: miRNA-1 expression; E: miRNA-200b; F: miRNA-145 expression. Compared to control group, *P<0.05.

pathway, cAMP signaling pathway, TNF signaling pathway and MAPK signaling pathway, as shown in **Figure 3B**.

Comparison of clinical characteristics of children with CKD and IKD

As shown in **Table 2**, Compared with children in the IKD group, children in the CKD group had significantly longer remission time of mucous hyperemia, erythema, hand and foot swelling, lymphadenectasis, and other symptoms (P< 0.05). The relative expression of miRNA-355 in CKD group and IKD group were (3.87±2.98) and (5.76±3.14); the relative expression levels of miRNA-2911 were (5.34±1.21) and (8.25± 4.36), respectively. Significant differences were found between the two groups.

Diagnostic value of miRNA-355 and miRNA-2911 in KD

Multivariate analysis of the eight factors obtained from comparison analysis showed that miRNA-355 and miRNA-2911 were independent predictors related to the diagnosis of KD, seen in **Table 3**. The cut-off value of miR-355 was 4.87, and the cut-off value of miR-2911 was 6.94. A scoring system for the diagnosis of KD were calculated using the following formula: Risk scores = (0.014 × expression value of miR-355) + (0.077 × expression value of miR-2911). As shown in **Figure 4** and **Table 4**, ROC showed that the sensitivity of miRNA-355 and miRNA-2911 for KD diagnosis were 73.8% and 71.2%, the specificity was 72.4% and 73.9%, and the AUCs were 0.793 and 0.757 respectively. As for the combined detection, the AUC for KD diagnosis could be increased to 0.806. This shows that miRNA-355 and miRNA-2911 have high diagnostic efficiency for KD.

Model validation risk of KD in children with high fever

Further, the predicted value was calculated through the Linear SVM analysis model and displayed in detail by using the discriminant diagram. As seen in **Figure 5**, the blue dot indicates the children with other febrile diseases, the red indicates the children with KD, and the diagonal is the discriminant line. It can be clearly seen that the children with KD and other febrile diseases can be distinguished by the discriminant line. There is only one sample discrimination error, so in the later improvement, it is considered that the grey area standard will be added, and 2-3 prediction models will be added to further improve the accuracy.

Discussion

Kawasaki disease (KD) is the main cause of acquired heart disease in children. It is an acute autoimmune vasculitis syndrome triggered by infection, which produces cellular inflammatory mediators and leads to vascular endothelial injury [11]. The clinical manifestations are acute fever, rash, red bayberry tongue,

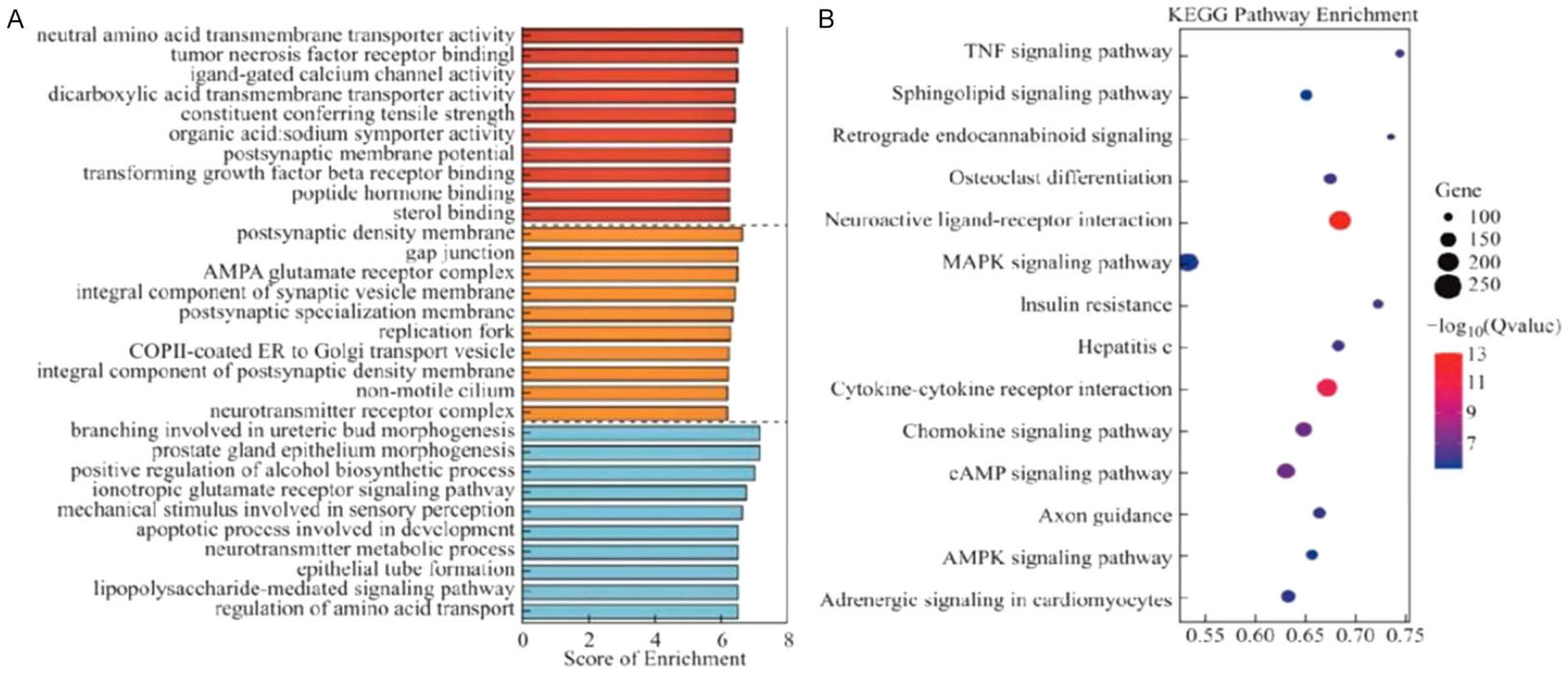

Figure 3. GO and KEGG Pathway analysis of the target differentially expressed miRNAs. A: GO analysis; B: KEGG Pathway analysis.

Table 2. Comparison of the clinical characteristics of the children with CKD and IKD

Index	CKD group (n=25)	IKD group (n=37)	χ^2/t	P
Gender			0.59	0.440
Male	17	23		
Female	8	14		
Age (years)	2.06±1.20	2.09±1.18	-0.145	0.884
Symptom regression (d)				
Mucous hyperemia	2.65±0.38	1.21±0.53	19.849	<0.001
Erythema	3.45±0.78	2.18±0.76	9.527	<0.001
Hand and foot swelling	3.38±1.01	2.12±1.05	7.183	<0.001
Lymphadenectasis	3.87±0.88	2.43±1.21	9.055	<0.001
WBC ($\times 10^9$/L)				
Pretherapy	16.48±5.13	16.17±4.79	0.357	0.721
Post-treatment	6.95±3.92	6.21±3.10	1.152	0.251
CK-MB (U/L)				
Pretherapy	158.64±23.87	231.84±39.84	-14.865	<0.001
Post-treatment	29.41±5.12	29.89±5.36	-0.538	0.591
NT-proBNP (ng/L)				
Pretherapy	398.64±98.41	1145.54±210.84	-32.165	<0.001
Post-treatment	86.87±29.14	91.46±30.20	-0.907	0.365
miRNA-355	3.87±2.98	5.76±3.14	-3.638	<0.001
miRNA-2911	5.34±1.21	8.25±4.36	-7.040	<0.001

Table 3. The results of multivariate analysis of factors for KD diagnosis

Parameters	β	OR (95% CI)	P
Symptom regression (d)			
Mucous hyperemia	0.495	1.59 (0.793-3.147)	0.156
Erythema	0.346	1.67 (0.813-3.428)	0.103
Hand and foot swelling	0.518	1.45 (0.835-2.569)	0.182
Lymphadenectasis	0.604	1.15 (0.297-3.376)	0.835
CK-MB (U/L)			
Pretherapy	0.592	0.79 (0.486-1.362)	0.335
NT-proBNP (ng/L)			
Pretherapy	0.616	1.15 (0.766-4.148)	0.259
miRNA-355	1.371	3.89 (1.612-4.339)	0.003
miRNA-2911	1.213	3.19 (1.715-5.147)	<0.001

oral mucosal congestion, but no oral ulcer, ocular conjunctival membrane congestion, or palmoplantar erythema. The incidence of KD is higher in male infants than that in females, with a higher rate in Japan. KD can lead to permanent damage of coronary arteries and eventually form a coronary aneurysm when it is serious, thus it has attracted wide attention of many newborn parents [12]. The standard treatment is intravenous immunoglobulin infusion combined with oral aspirin, which can alleviate fever and inflammation and reduce the incidence of coronary aneurysms. The understanding of Kawasaki disease has deepened, but how to reduce vascular inflammation and realize early diagnosis of Kawasaki disease is still the most urgent problem [13].

miRNA is an endogenous small RNA with a length of about 20~24 nucleotides. Several miRNAs can regulate the same gene. It can finely regulate the expression of a gene through the joint action of several miRNAs. It is speculated that miRNA regulates one-third of human genes. Many experiments have proved that miRNA is widely involved in cell growth and development, differentiation, metabolism and apoptosis, and is closely related to many human diseases [14]. Generally speaking, miRNA is considered to be an endogenous RNA that regulates gene expression at the post transcriptional level. However, recent studies have found that miRNA can be detected in routine blood testing, so it can be used as a detection index. Another benefit is that miRNA can withstand low temperature treatment and will

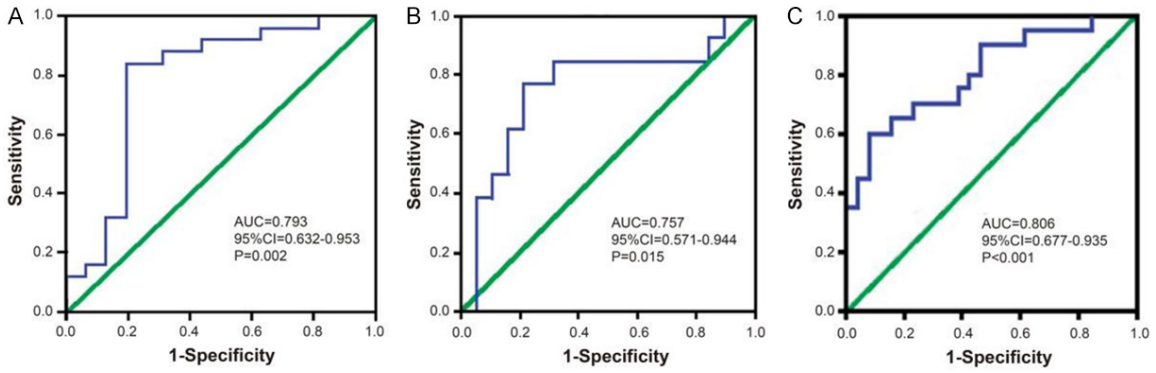

Figure 4. ROC curves of miRNA-355 and miRNA-2911 in diagnosing KD. A: Diagnostic efficacy of miRNA-355; B: Diagnostic efficacy of miRNA-2911; C: Diagnostic efficacy of miRNA-355 plus miRNA-2911.

Table 4. Diagnostic value of miRNA-355 and miRNA-2911 for KD

Index	Sensitivity	Specificity	AUC	95% CI	P
miRNA-355	73.8%	72.4%	0.793	0.632~0.953	<0.01
miRNA-2911	71.2%	73.9%	0.757	0.571~0.944	<0.05
Combined detection	83.6%	81.0%	0.806	0.677~0.935	<0.001

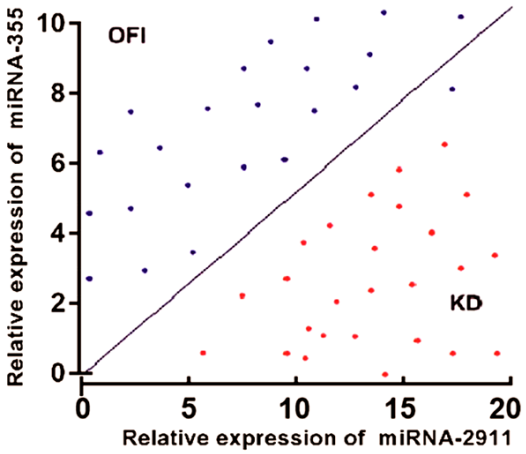

Figure 5. The validation of sample discriminant scatter plots.

not be destroyed by refrigeration, and stay relatively stable [15]. It is commonly used in clinical diagnosis of cardiovascular diseases. miRNA is a powerful regulator of cell life activities. It plays an important role in the occurrence, development, treatment and prognosis of diseases. It can exist stably in plasma and has obvious cell or tissue specificity. The detection of miRNA expression level in patients can assist the diagnosis of diseases and prediction of prognosis. Therefore, detecting the expression of plasma specific miRNA is a novel and simple method for the diagnosis of KD.

Piram et al. detected the expression of miRNA in the whole blood of children with KD in the acute phase and remission phase by high-throughput sequencing [16]. It was found that the expression of 41 miRNAs increased in children with KD in acute phase, including miRna-143, miRna-199, miRna-618, miRna-233, miRna-145, etc. It also found 63 differentially expressed miRNAs in the acute phase of KD children by the microarray analysis of KD children's plasma [17]. However, the efficacy of many differentially expressed miRNAs as KD diagnosis and treatment markers still needs further research. Chiba and other researchers detected the serum of children with Kawasaki disease and found that some miRNAs were significantly up-regulated versus normal healthy children. miRNA chip technology can effectively detect the expression profile of miRNA. RT-PCR technology is usually used to detect the expression of miRNA [18-20]. It can accurately detect the expression of its precursors. The operation is simple and convenient, and the reliability of the results is very high. The expression of miR-355 is very rich in macrophages and monocytes, which can reflect the regulatory changes of inflammation, especially in cardiovascular disease and hypercholesterolemia. Some studies found that miR-2911 was a biomarker of diabetes [21, 22]. Studies have found that the expression of miR-130a, miR-143, miR-145,

miR-223, miR-371 and miR-92a increased in patients with Kawasaki disease, and the expression of miR-21, miR-195, miR-1249 and miR-1260 decreased significantly in patients with Kawasaki disease. However, the mechanism of miRNA in Kawasaki disease remains to be clarified. Through next-generation sequencing technology, it was found that compared with Con group, 163 differentially expressed miRNAs were detected in the peripheral blood of children in the KD group, of which 126 were up-regulated and 49 were down-regulated. Hierarchical clustering showed that the miRNA profiles of children in KD group and Con group were significantly different, in which 10 miRNAs were significantly up-regulated and 4 miRNAs were down-regulated. This shows that the expression of miRNA in peripheral blood of children with Kawasaki disease is significantly different [23].

MiR-355 is a typical multifunctional miRNA. Studies have shown that miR-355 can regulate inflammatory infiltration, regulate autophagy, participate in immune response and other biological processes, and is related to cancer, cardiovascular disease and a variety of other diseases. Studies have shown that the expression of miR-355 is increased in children with dilated cardiomyopathy, and silencing miR-355 can inhibit pathological myocardial hypertrophy [19, 24]. The high expression of miR-355 is related to coronary atherosclerosis, and its expression is positively correlated with the injury degree of coronary artery stenosis. However, studies have shown that the expression of miR-155 in Kawasaki disease is reduced, probably because their study only detected the expression of miR-155 in regulatory T cells in patients with Kawasaki disease [25]. Moreover, miR-355 is a myocardial specific miRNA, and its diagnostic and therapeutic value in heart related diseases has been gradually confirmed. Some studies have found that the expression of miR-355 in serum of patients with acute myocardial infarction is elevated [26]. Studies have shown that the increased expression of miR-355 in acute myocardial infarction could cause vascular endothelial injury and inflammation [27]. It was found that the expression of miR-355 in peripheral blood could predict myocardial injury in cardiovascular diseases [28]. However, the roles of miR-355 in the development of Kawasaki disease were not reported in previous studies. Compared to other studies, the results of this study suggest that miR-355 could be used as a diagnostic marker of Kawasaki disease, but the exact mechanism of miR-355 in the development of Kawasaki disease is not clear, and further work is needed. miR-2911 is also a myocardial specific miRNA, which is involved in myocardial development and related diseases, such as myocardial hypertrophy and fibrosis. The presence of miR-2911 in the peripheral circulatory system has a potential predictive effect on myocardial lesions [29]. Studies have shown that the expression level of miR-2911 in serum of myocardial injury rats is significantly increased, and inhibiting the expression of miR-2911 in heart failure rats is conducive to the recovery of cardiac function and prolongation of the survival period [30]. Some studies have found that miR-2911 can be used as a diagnostic marker of acute myocardial infarction, and has high specificity and sensitivity [31]. Different from the above studies, this study investigated the predictive value of miR-2911 for diagnosis of Kawasaki disease, which was not done in previous studies.

In conclusion, our study found that the expression profile of miRNA in peripheral blood of children with Kawasaki disease was significantly disordered, and the expressions of miR-355 and miR-2911 were significantly up-regulated, and the combined detection of miR-355 and miR-2911 had a high diagnostic efficiency for Kawasaki disease. However, this study also has some limitations. First, the sample size of this study is limited. In the follow-up study, it is necessary to increase the sample size to improve its accuracy. Second, in future research, we can expand the sample collection area and carry out multi-center research with large sample size. Moreover, the function and mechanism of miRNA in patients with Kawasaki disease need to be explored in future research.

Disclosure of conflict of interest

None.

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