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MicroRNA-204 may predict the renal function in patients with chronic kidney disease

Guo Xiaoyun, BD[a], Li Hongjun, BD[b], Meng Cuijing, BD[c,*], Rong Li, BD[a], Zhang Mei, BD[d]

Abstract

Background: Chronic kidney disease significantly affects human health by loss of excretory kidney function. MicroRNAs have potential predictive and therapeutic significance for chronic kidney disease and fibrosis-related kidney diseases. This study aimed to investigate expression profiling and clinical significance of microRNA-204 (miR-204) expression in patients with chronic kidney disease.

Methods: A total of 126 patients with chronic kidney disease and age-matched 126 healthy controls were enrolled in this study. Blood samples were collected from participants and expression levels of miR-204 were detected using reverse transcription quantitative polymerase chain reaction. Expression of inflammatory cytokines in glomerular cells was measured using reverse transcription quantitative polymerase chain reaction. Inflammatory cytokines in serum were analyzed using enzyme-linked immunosorbent assay in all participants. Multivariate Cox-regression analysis was used to analyze the association between serum level of miR-204 and inflammation, renal fibrosis, and degree of chronic kidney disease.

Results: Chronic kidney disease patients had higher inflammatory cytokines including IL-1β, IL-6, TNF-α, IL-10, and IL-17 than healthy volunteers. Expression levels of inflammatory cytokines (IL-1β, IL-6, TNF-α, IL-10, and IL-17) were upregulated in patients with chronic kidney disease compared to healthy volunteers. Serum level of miR-204 was lower in chronic kidney disease patients than healthy patients. Expression of miR-204 was higher in healthy volunteers than patients with chronic kidney disease. In addition, expression of miR-204 was lower in glomerular cells in chronic kidney disease patients than those in the healthy volunteers. Furthermore, higher serum level of miR-204 was associated with better renal function in chronic kidney disease patients than patients who had lower serum level of miR-204. High serum levels of miR-204 were associated with degree of renal fibrosis and injury of chronic kidney disease patients. Multivariate Cox-regression analysis identified expression of miR-204 was positively correlated with inflammation in patients with chronic kidney disease.

Conclusion: Outcomes indicate that serum levels of miR-204 are downregulated in serum in patients with chronic kidney disease. Data suggest that serum levels of miR-204 can be used to evaluate the renal function in patients with chronic kidney disease.

Abbreviations: miR-204 = microRNA-204, miRNAs = microRNAs.

Keywords: chronic kidney disease, inflammation, miR-204, renal function

1. Introduction

Chronic kidney disease is one of global health problems and it is mainly caused by renal ischemia-reperfusion injury, sepsis, and nephrotoxicant.[1] Chronic kidney disease is characterized by deterioration in kidney function, inflammatory cell infiltration in renal tissue, and manifested by an increase in serum creatinine level.[2] Severity of chronic kidney disease depends on the function of glomerular cells and the status may vary based on chronicity.[3,4] Clinically, chronic kidney disease can slow deterioration of kidney function or persistent kidney dysfunction, which is associated with an irreversible loss of kidney cells and nephrons, and further leads to chronic kidney disease.[5] Hypoxic injury caused by oxidative stress injury in chronic kidney disease is thought to be the common underlying mechanism of chronic kidney disease regardless of the etiology of the kidney diseases.[6–8] Inflammation is the major underlying mechanism of glomerular cells dysfunction, and data show strong associations between glomerular cells dysfunction and risk of chronic renal failure.[9] Chronic kidney disease is associated with incident cardiovascular disease by

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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increasing inflammatory cytokines.[10] Therefore, inflammation is a potential target in the treatment of chronic kidney disease.

MicroRNAs (miRNAs), 20 to 22 long small noncoding RNA molecules, are associated with posttranscriptionally regulate gene expression in cells.[11] The role of miRNAs in controlling signaling pathways implicating in human diseases makes their application in diagnostics a powerful novel tool for the early detection, prognosis, and the development of innovative diseases therapies.[12] It has been found that miRNAs have emerged as an early-warning biomarker indicating the progression of chronic kidney disease.[13] Evidence has indicated that microRNA-204-5p (miR-204) upregulation alleviates inflammation and oxidative stress, which further decreases cell injury.[14] In addition, miR-204 impairs MUC4-dependent activation of the extracellular signal-regulated kinase signaling pathway and consequently ameliorates oxidative stress damage to renal tubular epithelial cells and prevents calcium oxalate kidney-stone formation.[15] Findings also suggest that miR-204 may play a protective role in high glucose-induced apoptosis and dysfunction in podocytes through down-regulation of Bdkrb2.[16] However, the role of miR-204 in the evaluation of the degree of chronic kidney disease has not been investigated in patients with chronic kidney disease. Therefore, it is important to investigate the role of miR-204 in evaluating the degree of renal fibrosis and injury in chronic kidney disease patients.

In this study, expression levels of miR-204 in serum and glomerular cells of patients with chronic kidney disease were investigated. This study also analyzed the corrections between miR-204 and renal function in patients with chronic kidney disease.

2. Methods

2.1. Participants

The cohort included chronic kidney disease patients (n = 126) and age and number-matched healthy controls (n = 126) were recruited in the Second Hospital of Tianjin Medical University between July 2021 and June 2022. This study was approved by the Ethic Committee of Second Hospital of Tianjin Medical University (Approval Number: 20210622RX1). Classification of patients with chronic kidney disease were defined according to available data regarding albuminuria as described previously,[17] and diagnosed by 3 doctors. Health controls were confirmed by routine physical examinations. Exclusion criteria were as follows: (1) age < 18 years; (2) patients with cancer history; (3) the estimated survival time <12 months; (4) patients with diabetic nephropathy; (5) patients with end-stage kidney disease; and (6) patients had prior kidney transplant or had < 2 serum creatinine levels during the admission. All patients gave written informed consent.

2.2. Parameters in participants

Parameters including body mass index, systolic blood pressure, diastolic blood pressure, triglyceride, total cholesterol, low-density lipoprotein, high density lipoprotein, high-sensitivity C-reactive protein, estimated glomerular filtration rate, and glycated hemoglobin were measured using standard method as described previously.[18]

2.3. Reverse transcription quantitative polymerase chain reaction

Total RNA was extracted from blood samples and renal tissues using RNeasy Mini kit (Invitrogen Life Technologies, Carlsbad, CA). RNA (500 ng) was reverse transcribed into cDNA using cDNA Synthesis Kit (Product code: 11117831001, Roche, Shanghai, China). Expression levels of IL-1β, IL-6, TNF-α, IL-10, and IL-17 were performed with specific primers and then measured using a SYBR-Green qRT-PCR assay (Takara Bio, Inc., Dalian, China). The primers used for gene expression assays were listed in Table 1. The results were analyzed using the comparative threshold cycle method. Target gene expression was normalized by glyceraldehyde 3-phosphate dehydrogenase.

2.4. Measurement of miR-204 expression

Total RNA was extracted from blood samples and renal tissues using RNeasy Mini kit (Invitrogen Life Technologies, Carlsbad, CA). Expression of miR-204 was analyzed using mirVana™ qRT-PCR miRNA measurement kit (Ambion, Austin, TX) according to the manufacture's instrument. The expression level of miR-148a was measured using a SYBR-Green qRT-PCR assay (Takara Bio, Inc.). The assays were performed in triplicate for all samples. RNU6B (catalog number 4440887, assay identifier 001093; Life Technologies) was used as the normalizer and miRNAs expression level was calculated using$2^{-\Delta Ct}$ as described previously.[19]

2.5. Enzyme-linked immunosorbent assay

Blood samples were obtained from chronic kidney disease patients and healthy volunteers. Serum level of IL-1β, IL-6, TNF-α, IL-10, and IL-17 were assessed using commercial enzyme-linked immunosorbent assay kit (Hycult Biotech, Uden, Netherlands) according to manufacturers' instrument.

2.6. Chronic kidney disease severity score

Chronic kidney disease severity score was evaluated according to Kidney Disease: Improving Global Outcomes criteria.[20] In brief, chronic kidney disease severity score in patients was determined by serum creatinine. 1 score: serum creatinine in patients increased 0.3 mg/dL within 48 hours or a 1.2 to 1.5 times from baseline within 7 days; 2 score: serum creatinine in patients increased 1.5 to 1.9 times increase in serum creatinine within 7 days; 3 score: serum creatinine in patients increased 1.9 to 2.9 times increase in serum creatinine within 7 days. 4 score: serum creatinine in patients increased 3.0 or more times increase in serum creatinine within 7 days.

Table 1

Sequences of primers were used in this study.

Gene name	Sequence	
IL-1	5′-GGCTGCTTCCAAACCTTTGA-3′	5′-GAAGACACGGATTCCATGGT-3′
IL-6	5′-GTGAGGAACAAGCCAGAG-3′	5′-TGACCAGAAGAAGGAATGC-3′
TNF-α	5′-CTAAGCGGAATCTCAATAGCG-3′	5′-GGGACTCTCAATCCTCGTC -3′
IL-10	5′-CAAGGCAGTGGAGCAGGTGAAG-3′	5′-GCTCTGTCTAGGTCCTGGAGTCC-3′
IL-17	5′-TGATGCTGTTGCTGCTGCTGAG-3′	5′-TGGAACGGTTGAGGTAGTCTGAGG-3′
GAPDH	5′-AACTTTGGCATTGTGGAAGG-3′	5′-GGATGCAGGGATGATGTTCT-3′

GAPDH = glyceraldehyde 3-phosphate dehydrogenase.

2.7. Statistical analysis

Data are expressed as mean ± standard deviation or n (%). Comparison of miR-204 level between chronic kidney disease patients and healthy controls was conducted by Wilcoxon rank sum test. Multivariate Cox-regression analysis was used to evaluate the correction between level of miR-204 and renal function. Data were analyzed using GraphPad Prism 6.0 (GraphPad Software Inc., San Diego, CA). The significance level was set at $P < .05$.

3. Results

3.1. Characteristic of patients with chronic kidney disease

A total of 126 chronic kidney disease patients and age-matched 126 healthy subjects were recruited and participated in this study. Baseline characteristics and biochemical parameters of each group are shown in Table 2. No obvious differences in age, number, gender, body mass index, systolic blood pressure, diastolic blood pressure, triglyceride, total cholesterol, and low-density lipoprotein-C and high density lipoprotein-C were observed between 2 groups ($P > .05$). However, compared with healthy controls, injury severity score, high-sensitivity C-reactive protein, glycated hemoglobin and Albuminuria were markedly increased in patients with chronic kidney disease, and estimated glomerular filtration rate was considerably reduced ($P < .05$). The flow diagram of this study is demonstrated in Figure 1.

3.2. Expression of miR-204 in chronic kidney disease patients

Serum level of miR-204 was compared between patients with chronic kidney disease and healthy controls. As shown in Figure 2A, chronic kidney disease patients had lower serum level of miR-204 than healthy volunteers ($P < .05$). Outcomes exhibited that expression level of miR-204 in kidney tissues was markedly downregulated in chronic kidney disease patients compared to those in healthy volunteers (1.44 ± 0.28 vs 4.60 ± 0.68, $P < .01$) (Fig. 2B). Reverse transcription quantitative polymerase chain reaction showed that the relative levels of miR-204 in the urine of the chronic kidney disease patients were significantly lower than those in the healthy control group (0.38 vs 3.22, $P < .05$; Fig. 2C).

3.3. Potential clinical diagnostic significance of miR-204 in chronic kidney disease patients

The clinical diagnostic of miR-204 was investigated based on the serum level of miR-204 in chronic kidney disease patients. The receiver operating characteristic curve demonstrated that miR-204 could use to diagnose chronic kidney disease patients from healthy individuals, with an area under the curve of 0.982, a sensitivity of 93.8%, and a specificity of 88.6% (Fig. 3). These data indicate that serum miR-204 has a high diagnostic value for patients with chronic kidney disease.

3.4. Associations between miR-204 and inflammatory factor in chronic kidney disease patients

Serum levels of inflammatory factors and associations between miR-204 and inflammatory factor were investigated in patients with chronic kidney disease. As shown in Figure 4A, chronic kidney disease patients had higher serum levels of IL-1β, IL-6, TNF-α, IL-10, and IL-17 than healthy volunteers. Outcomes also demonstrated that patients with chronic kidney disease presented relatively high mRNA levels of IL-1β, IL-6, TNF-α, IL-10, and IL-17 compared to healthy volunteers (Fig. 4B). A high inflammation score was observed in chronic kidney disease patients (Fig. 4C). Expression of miR-204 was negatively associated with the inflammation score in chronic kidney disease patients (Fig. 4D).

3.5. Associations between miR-204 and renal function in chronic kidney disease patients

Associations between miR-204 and renal function in chronic kidney disease patients were evaluated in this study. Higher serum

Table 2

Characteristics of patients with chronic renal injury.

Characteristic	Renal injury patients	Healthy control	*P* value
Number	126 (50.0%)	126 (50.0%)	–
Age (Years)	48.30 ± 10.35	48.35 ± 10.50	.97
Gender (n, %)			
Male	80 (63.5%)	82 (65.1%)	.92
Female	46 (36.5%)	44 (34.9%)	.94
BMI (kg/m^2)	25.46 ± 2.46	26.02 ± 2.60	.86
SBP (mm Hg)	78.57 ± 8.89	77.40 ± 7.92	.90
DBP (mm Hg)	116.44 ± 12.56	110.20 ± 10.32	.84
Kidney injury grade			
1	55	–	–
2	38	–	–
3	17	–	–
4	11	–	–
5	5	–	–
TC (mmol/L)	180.44 ± 20.07	176.60 ± 18.05	.80
LDL cholesterol (mg/dL)	110.84 ± 18.22	105.42 ± 15.29	.72
HDL cholesterol (mg/dL)	60.80 ± 10.18	64.28 ± 12.16	.83
TG	160.46 ± 12.51	167.52 ± 13.27	.87
Injury severity score	10.5 ± 3.4	–	–
hs-CRP (mg/L)	5.56 ± 0.76	0.42 ± 0.20	.004**
HbA1c (%)	9.01 ± 1.93	2.04 ± 0.72	.001**
eGFR	86.54 ± 12.67	101.40 ± 14.08	.022**
Albuminuria (mg/24 h)	7.94 ± 3.00	1.85 ± 0.50	.003**

BMI = body mass index, DBP = diastolic blood pressure, eGFR = estimated glomerular filtration rate, HbA1c = glycated hemoglobin, HDL = high density lipoprotein, hs-CRP = high-sensitivity C-reactive protein, LDL = low-density lipoprotein, SBP = systolic blood pressure, TC = total cholesterol, TG = triglyceride.

**$P < .01$.

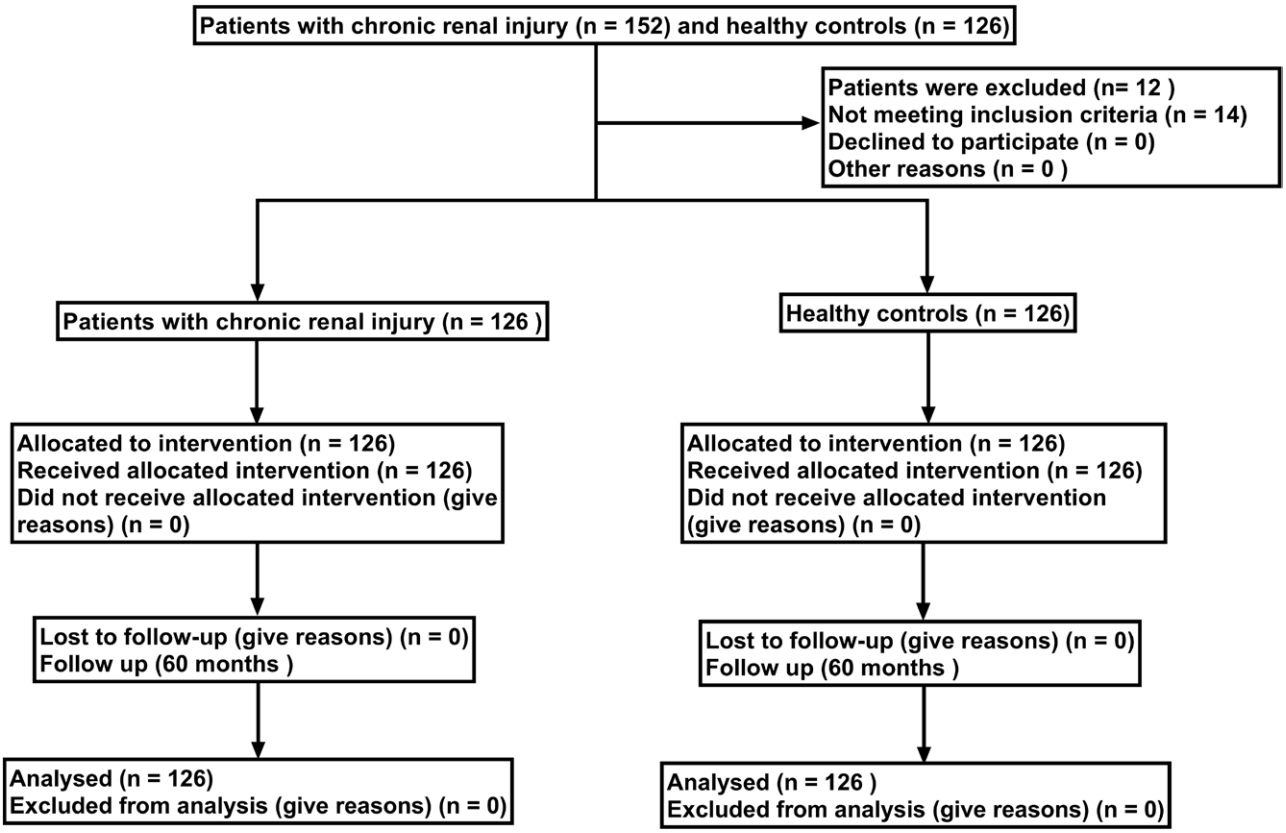

Figure 1. Flow diagram of the study design.

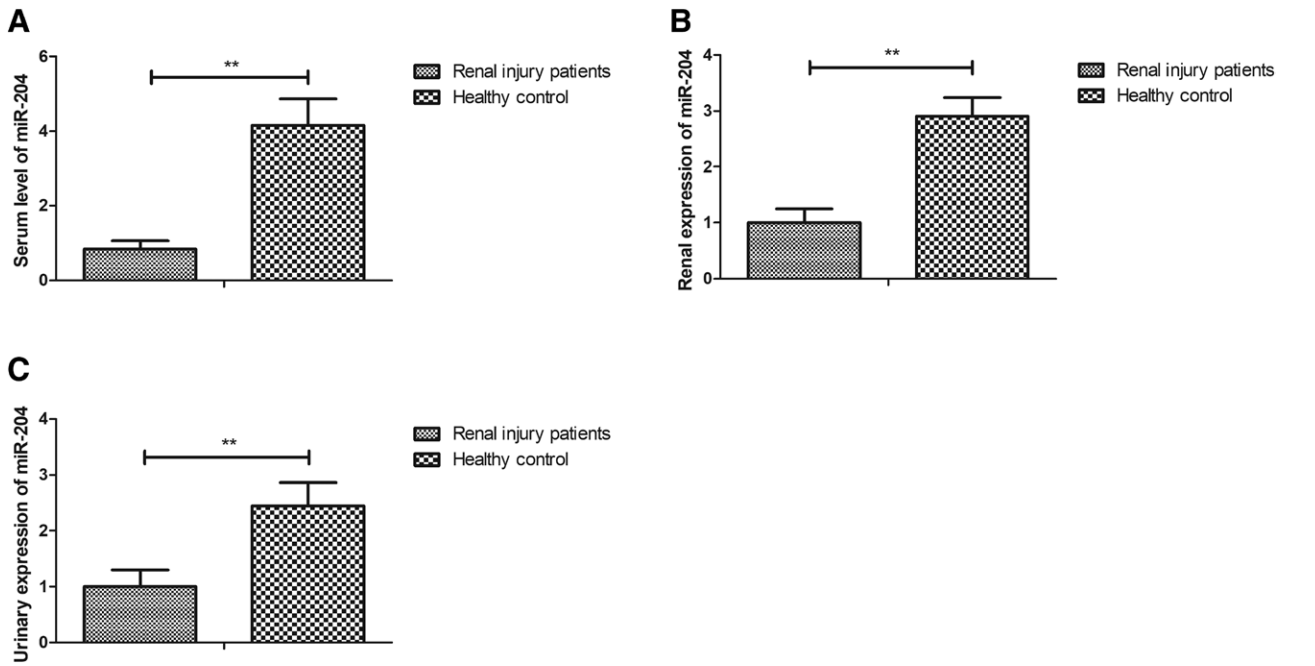

Figure 2. Expression of miR-204 in patients with chronic kidney disease. (A) Serum level of miR-204 in patients with chronic kidney disease and healthy volunteers. (B) Expression level of miR-204 in kidney tissues between chronic kidney disease patients and healthy volunteers. (C) Relative expression levels of miR-204 in the urine between chronic kidney disease patients and healthy volunteers. $^{**}P < .01$ vs patients with chronic kidney disease. miR-204 = microRNA-204.

levels of miR-204 were associated with better renal function in chronic kidney disease patients than patients who had lower serum miR-204 levels (Fig. 5A). Multivariate Cox-regression analysis identified that high serum level of miR-204 was associated with degree of renal fibrosis and injury of chronic kidney disease patients (Fig. 5B).

4. Discussion

Considerable evidence now indicates that inflammation plays a central role in the initiation and progression of chronic kidney disease.[21–23] miRNAs can alleviate sepsis-induced acute kidney injury by inhibiting renal inflammation.[24] Findings provide evidence of a prominent role for miR-204 in safeguarding the kidneys against common causes of chronic kidney disease.[25] In this study, we first examined the serum level of miR-204 and explored its diagnostic role in chronic kidney disease patients (Fig. 6). Outcomes suggest that serum miR-204 has a high diagnostic value for patients with chronic kidney disease. In addition, miR-204 can predict the degree of renal fibrosis and injury in patients with chronic kidney disease.

The clinical relevance of miR-204 in renal disease is supported by dysregulation of miR-204 in specimens obtained from patients with these diseases.[26] Findings show that sponging miR-204 provides a new mechanism to comprehend the pathogenesis of chronic kidney disease.[14] However, the association between miR-204 and renal function in chronic kidney disease patients has not been investigated, yet. This study demonstrated that serum level of miR-204 was downregulated in chronic kidney disease patients compared to healthy controls. Outcomes also have indicated that higher serum level of miR-204 is associated with better renal function, degree of renal fibrosis and injury of chronic kidney disease patients. Patients with chronic kidney disease frequently along with renal dysfunction.[27] Thus, clarifying the role and indication of renal function is important to manage chronic kidney disease patients. In this study, data found that the reduction of miR-204 was negatively correlated with renal function and positively correlated with estimated glomerular filtration rate, suggesting that miR-204 may be related to the degree of chronic kidney disease.

In recent years, miRNAs have been regarded as potential biomarkers of renal diseases due to its abundance, stability, and conservatism.[28] Early recognition and intervention of renal function are very important for reducing morbidity and mortality. In addition, numerous studies have demonstrated that inflammation is involved in the cascade of events that lead to chronic kidney disease.[2,29,30] Importantly, inflammation may predict kidney injury and early recognition of regulatory factor of inflammation contributes to the diagnosis and prognosis of chronic kidney disease patients.[31] Here, we observed that levels of inflammatory factors increased by the reduction of miR-204, which might be a potential biomarker of chronic kidney disease. Further studies suggested that miR-204 protects against chronic kidney disease via the regulation of several targets with roles in inflammation and fibrosis.[25,26,32] Consistent with these reports, patients with chronic kidney disease showed lower levels of miR-204 and higher levels of inflammatory cytokines, which were negatively associated with degree of renal fibrosis and injury of chronic kidney disease patients.

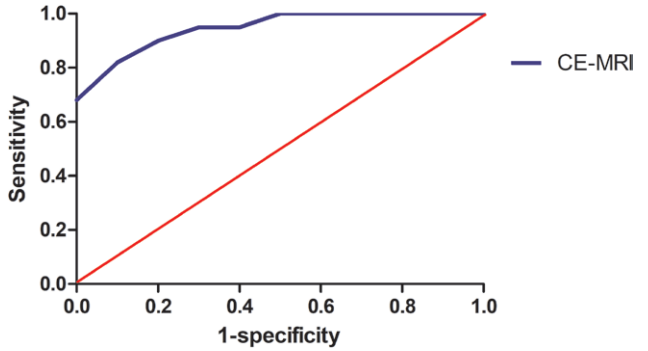

Figure 3. ROC curve analyzed the sensitivity and specificity miR-204 for patients with chronic kidney disease. miR-204 = microRNA-204, ROC = receiver operating characteristic.

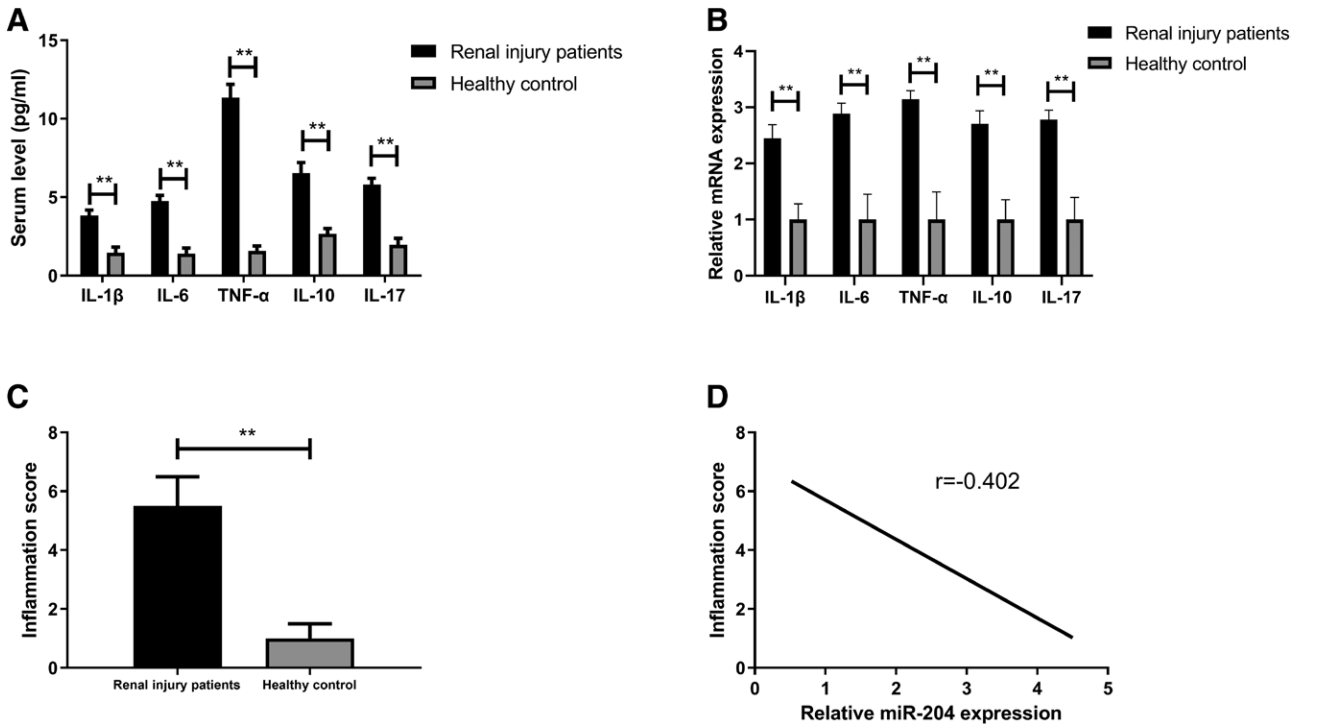

Figure 4. Associations between miR-204 and inflammatory factor in chronic kidney disease patients. (A) Serum inflammatory cytokines IL-1β, IL-6, TNF-α, IL-10, and IL-17 in chronic kidney disease patients. (B) mRNA level of IL-1β, IL-6, TNF-α, IL-10, and IL-17 in renal tissue in chronic kidney disease patients. (C) Inflammation score between chronic kidney disease patients and healthy volunteers. (D) Associations between serum of miR-204 and inflammation score in chronic kidney disease patients. $^{**}P < .01$ vs patients with chronic kidney disease. miR-204 = microRNA-204.

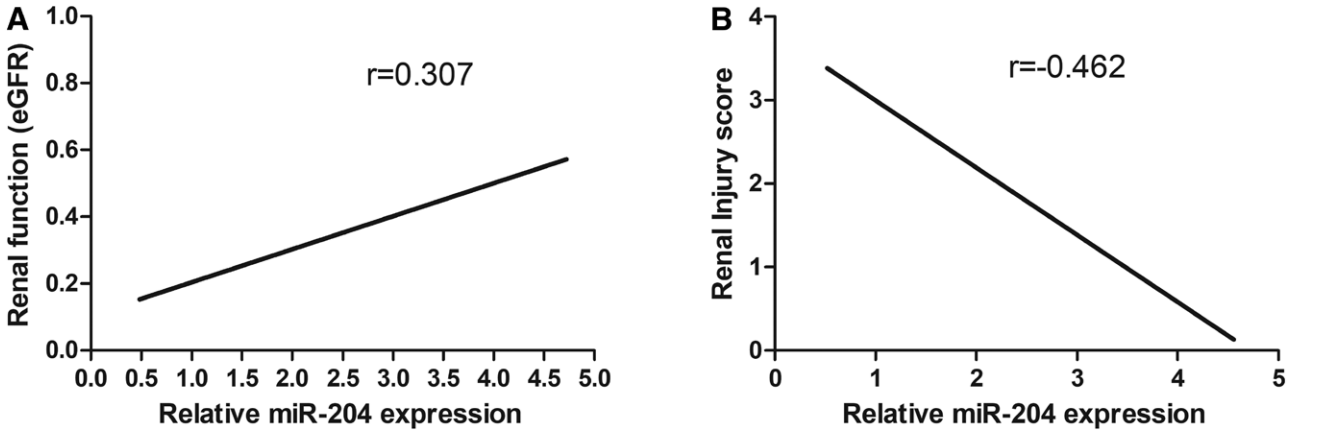

Figure 5. Associations between miR-204 and renal function in chronic kidney disease patients. miR-204 = microRNA-204. (A) Associations between miR-204 and renal function in chronic kidney disease patients. (B) Associations between miR-204 and renal injury in chronic kidney disease patients. miR-204 = microRNA-204.

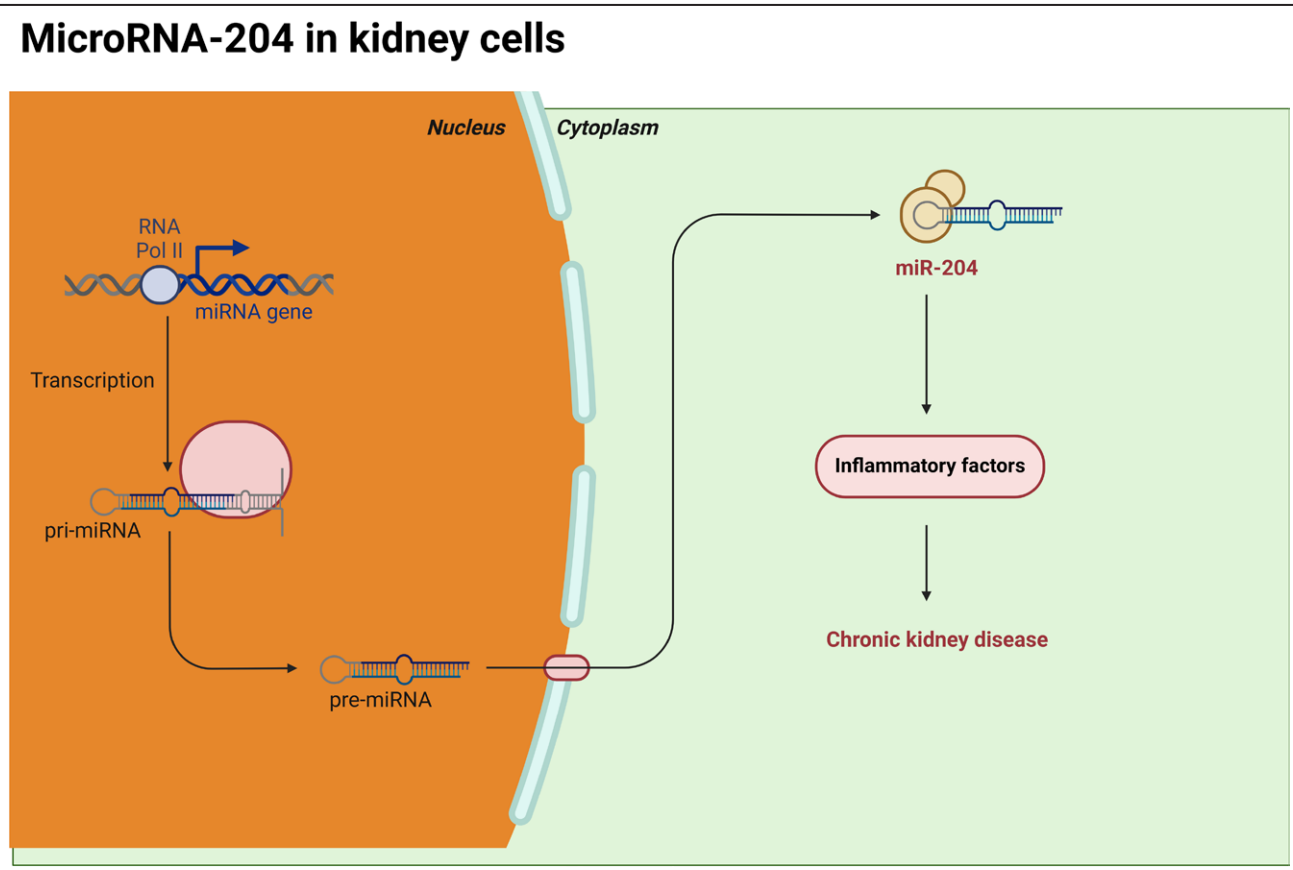

Figure 6. miR-204 in chronic kidney disease. miR-204 = microRNA-204.

The miR-19b plays a critical pathologic role in tubulointerstitial inflammation, representing a new therapeutic target for kidney disease.[33] In addition, inhibiting miR-214-3p would alleviate tubular epithelial cell ferroptosis in cis-AKI via GPX4.[34] Data in this study showed that miR-204 expression was associated with inflammatory cytokines expression in chronic kidney disease patients. Furthermore, miR-373 exacerbates renal injury and fibrosis, which may provide a potential therapeutic strategy for renal fibrosis.[35] This study found that the level of miR-204 could identify chronic kidney disease patients from healthy individuals, which had a high clinical diagnostic value. Notably, outcomes in this study found that miR-204 may be useful factors to predict inflammation for chronic kidney disease patients. The reduction of miR-204 may indicate who have inflammation derived from chronic kidney disease. We also indicated that expression of miR-204 was negatively associated with the inflammation score in chronic kidney disease patients. Additionally, we also recognize that there are some limitations in the current study. It is necessary to further understand the role of miR-204 in diagnosis of renal function and analyze the associations with chronic kidney disease in more patients in our future study.

Several limitations should be addressed. First, the number of samples was few and performed at a single center in China. Second, this study did not measure the levels of miR-204 before and after kidney injury to determine whether miR-204 can serve

as a representative marker for kidney damage and recovery. Third, the study did not collect the data on miR-204 expression in renal tissue. Therefore, further study with histological data should be investigated in patients with chronic kidney disease in more clinical samples.

5. Conclusion

In conclusion, findings in the current study indicate that serum level of miR-204 is a potential diagnostic biomarker for patients with chronic kidney disease. Serum level of miR-204 is negatively associated with the degree of renal fibrosis and positively associated with renal function in chronic kidney disease patients. This study suggests that miR-204 may be a promising diagnostic marker in patients with chronic kidney disease.

Author contributions

Conceptualization: Guo Xiaoyun, Li Hongjun, Rong Li, Zhang Mei.
Data curation: Guo Xiaoyun, Li Hongjun, Meng Cuijing, Rong Li, Zhang Mei.
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Validation: Meng Cuijing, Rong Li.
Visualization: Meng Cuijing, Rong Li.
Writing – original draft: Meng Cuijing, Rong Li.
Writing – review & editing: Rong Li.

References

[1] Zha D, Yang X, Zhang H, et al. Development and validation of prediction model using nursing notes on sentiment scores for prognosis of patients with severe acute kidney injury receiving continuous renal replacement therapy based on computational intelligence algorithms. Ann Transl Med. 2022;10:1110.
[2] Thongnak L, Jaruan O, Pengrattanachot N, et al. Resistant starch from black rice, Oryza sativa L. var. ameliorates renal inflammation, fibrosis and injury in insulin resistant rats. Phytother Res. 2022;37:935–48.
[3] Ganipisetti VM, Dudiki N, Athavale A, Bollimunta P, Maringanti BS. Daptomycin-rifampin-induced rhabdomyolysis, acute renal failure, and hepatic injury: a case report and literature review. Cureus. 2023;15:e36834.
[4] Upamalika S, Wannige CT, Vidanagamachchi SM, et al. A review of molecular mechanisms linked to potential renal injury agents in tropical rural farming communities. Environ Toxicol Pharmacol. 2022;92:103850.
[5] Klein SJ, Brandtner AK, Lehner GF, et al. Biomarkers for prediction of renal replacement therapy in acute kidney injury: a systematic review and meta-analysis. Intensive Care Med. 2018;44:323–36.
[6] Tominaga T, Sharma I, Fujita Y, Doi T, Wallner AK, Kanwar YS. Myo-inositol oxygenase accentuates renal tubular injury initiated by endoplasmic reticulum (Er) stress. Am J Physiol Renal Physiol. 2018;316:301.
[7] van den Berg MF, Schoeman JP, Defauw P, et al. Assessment of acute kidney injury in canine parvovirus infection: comparison of kidney injury biomarkers with routine renal functional parameters. Vet J. 2018;242:8–14.
[8] Waasdorp M, de Rooij DM, Florquin S, Duitman J, Spek CA. Protease-activated receptor-1 contributes to renal injury and interstitial fibrosis during chronic obstructive nephropathy. J Cell Mol Med. 2018;23:1268–79.
[9] Hanberg JS, Rao VS, Ahmad T, et al. Inflammation and cardio-renal interactions in heart failure: a potential role for interleukin-6. Eur J Heart Fail. 2018;20:933–4.
[10] Yuan Q, Wang J, Peng Z, et al. Neutrophil-to-lymphocyte ratio and incident end-stage renal disease in Chinese patients with chronic kidney disease: results from the Chinese cohort study of chronic kidney disease (C-STRIDE). J Transl Med. 2019;17:86.
[11] Zaman A, Banday AA. Angiotensin (1-7) protects against renal ischemia-reperfusion injury via regulating expression of NRF2 and microRNAs in fisher 344 rats. Am J Physiol Renal Physiol. 2022;323:F33–47.
[12] Wu YL, Li HF, Chen HH, Lin H. MicroRNAs as biomarkers and therapeutic targets in inflammation- and ischemia-reperfusion-related acute renal injury. Int J Mol Sci . 2020;21:6738.
[13] Phulkerd T, Lertussavavivat T, Limothai U, et al. Circulating and urinary microRNAs profile for predicting renal recovery from severe acute kidney injury. J Intensive Care. 2022;10:45.
[14] Qiu B, Qi X, Wang J. CircTLK1 downregulation attenuates high glucose-induced human mesangial cell injury by blocking the AKT/NF-kappaB pathway through sponging miR-126-5p/miR-204-5p. Biochem Genet. 2022;60:1471–87.
[15] Xie Z, Chen J, Chen Z. MicroRNA-204 attenuates oxidative stress damage of renal tubular epithelial cells in calcium oxalate kidney-stone formation via MUC4-mediated ERK signaling pathway. Urolithiasis. 2022;50:1–10.
[16] Han X, Li Q, Wang C, Li Y. MicroRNA-204-3p attenuates high glucose-induced MPC5 podocytes apoptosis by targeting braykinin B2 receptor. Exp Clin Endocrinol Diabetes. 2019;127:387–95.
[17] de Boer IH, Khunti K, Sadusky T, et al. Diabetes management in chronic kidney disease: a consensus report by the American diabetes association (ADA) and kidney disease: improving global outcomes (KDIGO). Kidney Int. 2022;102:974–89.
[18] Korbut AI, Romanov VV, Klimontov VV. Urinary markers of tubular injury and renal fibrosis in patients with type 2 diabetes and different phenotypes of chronic kidney disease. Life (Basel). 2023;13:343.
[19] Shiels A. TRPM3_miR-204: a complex locus for eye development and disease. Hum Genomics. 2020;14:7.
[20] Rodrigues N, Branco C, Costa C, et al. Acute kidney injury in autologous hematopoietic stem cell transplant for patients with lymphoma - KDIGO classification with creatinine and urinary output criteria: a cohort analysis. Ren Fail. 2023;45:2183044.
[21] Han F, Gao Y, Ding CG, et al. Knockdown of NLRC5 attenuates renal I/R injury in vitro through the activation of PI3K/Akt signaling pathway. Biomed Pharmacother. 2018;103:222–7.
[22] Ergin B, Zuurbier CJ, Bezemer R, et al. Ascorbic acid improves renal microcirculatory oxygenation in a rat model of renal I/R injury. J Transl Int Med. 2015;3:116–25.
[23] Todorovic Z, Medic B, Basta-Jovanovic G, et al. Acute pretreatment with chloroquine attenuates renal I/R injury in rats. PLoS One. 2014;9:e92673.
[24] Ding C, Ding X, Zheng J, et al. miR-182-5p and miR-378a-3p regulate ferroptosis in I/R-induced renal injury. Cell Death Dis. 2020;11:929.
[25] Cheng Y, Wang D, Wang F, et al. Endogenous miR-204 protects the kidney against chronic injury in hypertension and diabetes. J Am Soc Nephrol. 2020;31:1539–54.
[26] Liu J, Liu Y, Wang F, Liang M. miR-204: molecular regulation and role in cardiovascular and renal diseases. Hypertension. 2021;78:270–81.
[27] Shariat SF, Jenkins A, Roehrborn CG, Karam JA, Stage KH, Karakiewicz PI. Features and outcomes of patients with grade IV renal injury. BJU Int. 2008;102:728–33; discussion 733.
[28] Gan XG, Wang ZH, Xu HT. Mechanism of miRNA-141-3p in calcium oxalate-induced renal tubular epithelial cell injury via NLRP3-mediated pyroptosis. Kidney Blood Press Res. 2022;47:300–8.
[29] Zhang N, Guan C, Liu Z, et al. Calycosin attenuates renal ischemia/reperfusion injury by suppressing NF-kappaB mediated inflammation via PPARgamma/EGR1 pathway. Front Pharmacol. 2022;13:970616.
[30] Ma R, He Y, Fang Q, Xie G, Qi M. Ferulic acid ameliorates renal injury via improving autophagy to inhibit inflammation in diabetic nephropathy mice. Biomed Pharmacother. 2022;153:113424.
[31] Bezerra GF, Meneses GC, Jacinto VN, et al. Preliminary study for new markers of early tubuloglomerular injury and renal inflammation in patients with visceral leishmaniasis receiving liposomal amphotericin B treatment. Am J Trop Med Hyg. 2022;106:1191–5.
[32] Mahtal N, Lenoir O, Tinel C, Anglicheau D, Tharaux PL. MicroRNAs in kidney injury and disease. Nat Rev Nephrol. 2022;18:643–62.
[33] Lv LL, Feng Y, Wu M, et al. Exosomal miRNA-19b-3p of tubular epithelial cells promotes M1 macrophage activation in kidney injury. Cell Death Differ. 2020;27:210–26.
[34] Zhou J, Xiao C, Zheng S, et al. MicroRNA-214-3p aggravates ferroptosis by targeting GPX4 in cisplatin-induced acute kidney injury. Cell Stress Chaperones. 2022;27:325–36.
[35] Yang H, Liao D, Tong L, Zhong L, Wu K. MiR-373 exacerbates renal injury and fibrosis via NF-kappaB/MatrixMetalloproteinase-9 signaling by targeting Sirtuin1. Genomics. 2019;111:786–92.