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MiR-107 as a Biomarker Predicts Cardiac Hypertrophy in Chronic Hemodialysis Patients

ABSTRACT

Background: Maintenance hemodialysis (MHD) can lead to hypertrophy of myocardial cells and interstitial fibrosis in patients, which can ultimately culminate in left ventricular hypertrophy (LVH). The objective of this study is to examine the expression of miR-107 in patients undergoing MHD who also present with LVH and to evaluate its predictive value.

Methods: A total of 135 patients with end-stage renal disease who were undergoing MHD were included as the research subjects. Patients were grouped based on left ventricular mass index. Real-time quantitative polymerase chain reaction was used to detect the expression of miR-107 in the serum of the patients. The receiver operating characteristic curve was used to evaluate the diagnostic value of miR-107 in MHD with LVH patients. The Pearson's method was used for correlation analysis. Logistic regression model was used to analyze the risk factors for cardiac hypertrophy in MHD patients.

Results: Serum miR-107 is highly expressed in patients with MHD and LVH, and it may be a potential diagnostic biomarker. miR-107 has relatively high sensitivity and specificity in predicting LVH in patients with MHD. Serum miR-107 is closely related to the serum high-sensitivity C-reactive protein level and echocardiographic characteristics of patients with MHD combined with LVH. MiR-107 correlates with echocardiographic characteristics of MHD patients with LVH. Finally, logistic regression analysis indicated that miR-107 was a risk factor for LVH in MHD patients.

Conclusion: Serum miR-107 may have significant potential in diagnosing cardiac hypertrophy in MHD patients and is a potential biological indicator for cardiac hypertrophy in MHD patients.

Keywords: Diagnosis, left ventricular hypertrophy, maintenance hemodialysis, miR-107

INTRODUCTION

Chronic kidney disease (CKD) constitutes a significant global public health challenge.[1] Hemodialysis (HD) stands as the cornerstone of renal replacement therapy, playing a critical role in extending survival and enhancing the quality of life for patients.[2] End-stage renal disease (ESRD) represents a severe and irreversible deterioration of kidney function, necessitating long-term maintenance hemodialysis (MHD) as the disease progresses.[3] Patients undergoing MHD frequently contend with a myriad of complications, including hypertension, volume overload, the accumulation of uremic toxins, and disorders of mineral metabolism. These conditions can precipitate myocardial cell hypertrophy and interstitial fibrosis, leading to the development of left ventricular hypertrophy (LVH).[4] Cardiac hypertrophy frequently arises due to sustained pressure overload or underlying pathological conditions and can ultimately progress to deleterious heart failure, which is a notable clinical risk factor for mortality.[5] Consequently, it is of paramount importance to investigate the onset and progression of LVH in MHD patients, as well as to identify innovative, cost-effective, and clinically relevant biomarkers for early detection.

In recent years, a growing body of evidence has elucidated the role of microRNA (miRNA) molecules in the regulation of various diseases, including cardiac hypertrophy.[6-8] MiR-590-5p has been implicated in the pathological hypertrophy associated with heart failure.[9] Research has identified serum miR-27b as a promising

ORIGINAL INVESTIGATION

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biomarker for the screening of LVH.[10] Furthermore, it has been demonstrated that miR-133a is expressed at diminished levels in the hearts of patients with maintenance hemodialysis (MHD) who exhibit cardiac hypertrophy.[11] Among the members of the miRNA family, miR-107 has garnered attention for its involvement in a diverse array of pathological and physiological processes, including cell proliferation, apoptosis, metabolism, and fibrosis.[12] Recent studies have revealed that miR-107 is aberrantly expressed in cardiovascular diseases, such as myocardial hypertrophy and heart failure.[13]

Previous studies have indicated a potential role for miR-107 in the development of cardiac hypertrophy. However, the specific expression and association of miR-107 in MHD-induced cardiac hypertrophy remain largely uncharted. Therefore, this research endeavor seeks to investigate the expression levels and predictive significance of miR-107 in MHD with LVH patients.

METHODS

General Information

A total of 135 patients with ESRD who underwent MHD treatment at The First Affiliated Hospital of Guizhou University of Traditional Chinese Medicine between February 2023 and February 2024 were selected for this study. The criteria for inclusion encompassed: a confirmed diagnosis of ESRD; a minimum of 3 months of MHD treatment; willingness to participate in the study, with a duly signed informed consent form. The exclusion criteria included: irregularities in dialysis or inadequate volume management; unstable medical conditions such as malignant hypertension or acute infections; coexisting malignant tumors; presence of active systemic infections; recent cardiovascular events occurring within the past 3 months; and cases of chronic inflammation, hematological disorders, or significant hepatic dysfunction. Furthermore, all patients were excluded from special types of LVH, such as cardiac amyloidosis and Fabry disease, through clinical evaluation, laboratory tests, and imaging examinations. This research has received ethical approval from the Medical Ethics Committee of The First Affiliated Hospital of Guizhou University of Traditional Chinese Medicine (Date: June 8, 2022; No. 20220101). This article did not use artificial intelligence–assisted technology.

Treatment and Nursing

The Prirnus1350 dialyzer, manufactured in the USA, is designed as a disposable device. It features a membrane composed of polysulfone, with a membrane area ranging from 1.2 to 1.6 m^2. The dialysate water is sourced from a reverse osmosis system, utilizing standard bicarbonate dialysate. The dialysate flow rate is maintained at 500 mL/min, while the blood flow rate is set between 200 and 300 mL/min. Patients typically undergo HD 3 times a week, with each session lasting 4 hours. During this process, anticoagulation therapy is administered, employing either unfractionated heparin or low molecular weight heparin.

The patient receives consistent and comprehensive care, with a strong emphasis on dietary management. Hemodialysis treatments are meticulously conducted in adherence to established medical protocols, which encompass the determination of dialysis frequency, the careful selection of dialysate, and the vigilant maintenance of vascular access. General nursing practices involve the routine monitoring of patients' physiological parameters to detect any changes in renal function, allowing for timely adjustments to treatment plans. In the realm of health education, nursing staff provide patients with essential knowledge regarding HD, ensuring they are equipped with a fundamental understanding of their condition. Dietary guidance is tailored to restrict high-potassium and high-phosphorus foods, as well as managing fluid intake, thereby alleviating discomfort and minimizing potential risks during the inter-dialytic period. Management of pharmacotherapy is equally critical and involves the careful control of hypertension, the management of anemia, and the regulation of phosphate levels, ensuring that all medications administered do not exacerbate renal impairment. Complementing these medical and dietary interventions, psychological support is an integral component of care, wherein nursing staff offer personalized explanations of self-management strategies, tailored to each patient's psychological state.

Survey Indicators

Basic information such as sex, age, body mass index (BMI), medical history, MHD duration, and drug use were recorded. Diagnosis of diabetes was established based on criteria that included recent utilization of hypoglycemic agents, fasting blood glucose levels exceeding 126 mg/dL, random blood glucose levels surpassing 200 mg/dL, and/or a glycosylated hemoglobin (HbA1c) percentage of 6.5% or higher. The most important biochemical indicators of the patients were collected as well. A fasting blood specimen was collected from each patient, and serum was subsequently separated for future analyses.

Grouping of Patients

All patients underwent comprehensive transthoracic echocardiography, which was employed to assess key cardiac parameters, including interventricular septum thickness (IVST), left ventricular posterior wall thickness (LVPWT), left ventricular diastolic dimension (LVDD), and left ventricular systolic diameter. Patients were categorized into 2 distinct groups based on their left ventricular mass index (LVMI) values: those exhibiting LVH during MHD (MHD with LVH group) and those who did not exhibit LVH (MHD without LVH group). Left ventricular hypertrophy was defined according to sex-specific criteria, with LVMI values exceeding 125 g/m^2 for male

HIGHLIGHTS

- Serum miR-17-5p expression is upregulated in maintenance hemodialysis (MHD) patients with left ventricular hypertrophy (LVH).
- MiR-107 has a high sensitivity and specificity in predicting MHD patients with LVH.
- MiR-107 is closely related to the inflammation and echocardiographic features of patients with MHD and LVH.
- MiR-107 was a risk factor for LVH in MHD patients.

patients and 115 g/m^2 for female patients.[14,15] The Devereux formula was employed to compute LVMI,[16] with left ventricular mass (LVM) calculated as follows: LVM (g) = 0.8 × [1.04 × (LVDD + IVST + LVPWT)^3 – (LVDD)^3] + 0.6. Subsequently, LVMI is derived from the patient's measured body surface area (BSA) using the equation: LVMI (g/m^2) = LVM/BSA. The BSA is calculated using the following formula: BSA (m^2) = [0.0061 × height (cm) + 0.0128 × weight (kg)] – 0.1529.

Real-Time Quantitative Polymerase Chain Reaction

Total RNA was meticulously extracted from serum utilizing TRIzol RNA Extraction Reagent (Life Technologies). Subsequently, complementary DNA (cDNA) was synthesized employing the Swe-Script RT II First Strand cDNA Synthesis Reagent Kit (Service Bio). Real-time quantitative polymerase chain reaction (RT-qPCR) was performed with the 2 × SYBR Green qPCR Master Mix (Service Bio) on the Step One Real-Time PCR System (Life Technologies). Each assay was conducted in triplicate, and the final results were calculated based on U6 as the internal reference for determining the relative expression levels of miR-107.

Statistical Methods

Data analysis was conducted using SPSS version 26.0 software. To assess differences between groups, independent samples analysis of variance was employed for normally distributed measurement data, while the Kruskal–Wallis test was utilized for non-normally distributed data. For categorical data, the chi-squared test was implemented. Correlation analysis was performed using Pearson's method. The diagnostic value of miR-107 in patients with cardiac hypertrophy undergoing MHD was evaluated through receiver operating characteristic (ROC) curve analysis. A multivariate logistic regression model was applied to examine the risk factors associated with cardiac hypertrophy in MHD patients. All statistical analyses were executed with a two-tailed test, and a significance level of $P < .05$ was established.

RESULTS

Comparative Clinical Data Between the Two Groups

In a cohort of 135 patients undergoing MHD, a notable 62.2% (84 patients) were found to have developed LVH. The study encompassed a total of 135 MHD patients, categorized into 2 distinct groups: MHD without LVH group (n = 51) and MHD with LVH group (n = 84). There was no statistically significant difference in age, gender, BMI, underlying diseases, MHD duration, and information on medication use between the 2 groups ($P > .05$) (Table 1).

However, the levels of parathyroid hormone (PTH), total serum cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) were significantly elevated in the MHD patients with LVH compared to those without LVH, with the differences reaching statistical significance ($P < .05$) (Table 2).

Expression and Diagnostic Significance of MiR-107 in Maintenance Hemodialysis with Left Ventricular Hypertrophy Patients

The results of the RT-qPCR analysis revealed no significant differences in serum miR-107 expression pre- and post-first dialysis in the patient cohort ($t = 1.570$, $P = .118$) (Figure 1A).

Table 1. General Information on Chronic Hemodialysis Patients

Variables	MHD Without LVH (n = 51)	MHD with LVH (n = 84)	*t*	*P*
Age (years)	53.25 ± 9.89	55.05 ± 12.27	0.883	.379
Sex (male/female)	21/30	43/41	1.127	.262
BMI (kg/m^2)	20.50 ± 1.44	21.07 ± 3.29	1.161	.248
Hypertension (yes/no)	19/32	38/46	0.907	.366
Diabetes (yes/no)	12/39	29/65	1.346	.181
MHD duration (months)	83.84 ± 37.49	96.70 ± 52.80	1.521	.131
Drug [n (%)]			0.585	.560
Calcium inhibitors	18 (35.3)	33 (39.3)		
ACE inhibitors	11 (21.6)	20 (22.6)		
AT IIr inhibitors	8 (15.7)	10 (13.1)		
β-Blockers	14 (27.4)	21 (25.0)		

ACE, angiotensin-converting enzyme; AT IIr, angiotensin II receptor; BMI, body mass index; LVH, left ventricular hypertrophy; MHD, maintenance hemodialysis; β-Blockers, β receptor blocker.

Notably, the serum miR-107 levels were significantly elevated in the MHD with LVH group compared to those without LVH ($t = 10.500$, $P < .001$) (Figure 1B). Furthermore, the ROC curve analysis demonstrated that miR-107 serves as an effective predictor for MHD with LVH. The optimal diagnostic cut-off value of miR-107 in predicting LVH in MHD patients was 1.15, with a sensitivity of 86.9%, a specificity of 82.4%, and an area under the curve of 0.905 (95% CI: 0.855-0.954, $P < .001$) (Figure 1C).

Analysis of the Correlation Between MiR-107 and the Inflammatory Marker High-Sensitivity C-Reactive Protein

The serum level of high-sensitivity C-reactive protein (hs-CRP) in MHD patients with LVH was significantly higher

Table 2. Biochemical Characteristics of Chronic Hemodialysis Patients

Variables	MHD Without LVH (n = 51)	MHD with LVH (n = 84)	*t*	*P*
Hemoglobin (g/dL)	9.12 ± 0.67	9.29 ± 0.76	1.341	.182
Albumin (g/dL)	4.21 ± 0.46	4.31 ± 0.58	1.019	.310
PTH (pg/mL)	185.71 ± 63.41	223.05 ± 87.08	2.662	.009**
TC (mmol/L)	6.73 ± 0.79	7.09 ± 0.62	2.909	.004**
TG (mmol/L)	6.78 ± 0.71	7.25 ± 2.14	1.489	.139
HDL-C (mmol/L)	2.22 ± 0.56	2.12 ± 0.37	1.292	.199
LDL-C (mmol/L)	4.28 ± 0.98	4.84 ± 0.95	3.277	.001**

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVH, left ventricular hypertrophy; MHD, maintenance hemodialysis; PTH, parathyroid hormone; TC, serum total cholesterol; TG, triglycerides.
**$P < .01$.

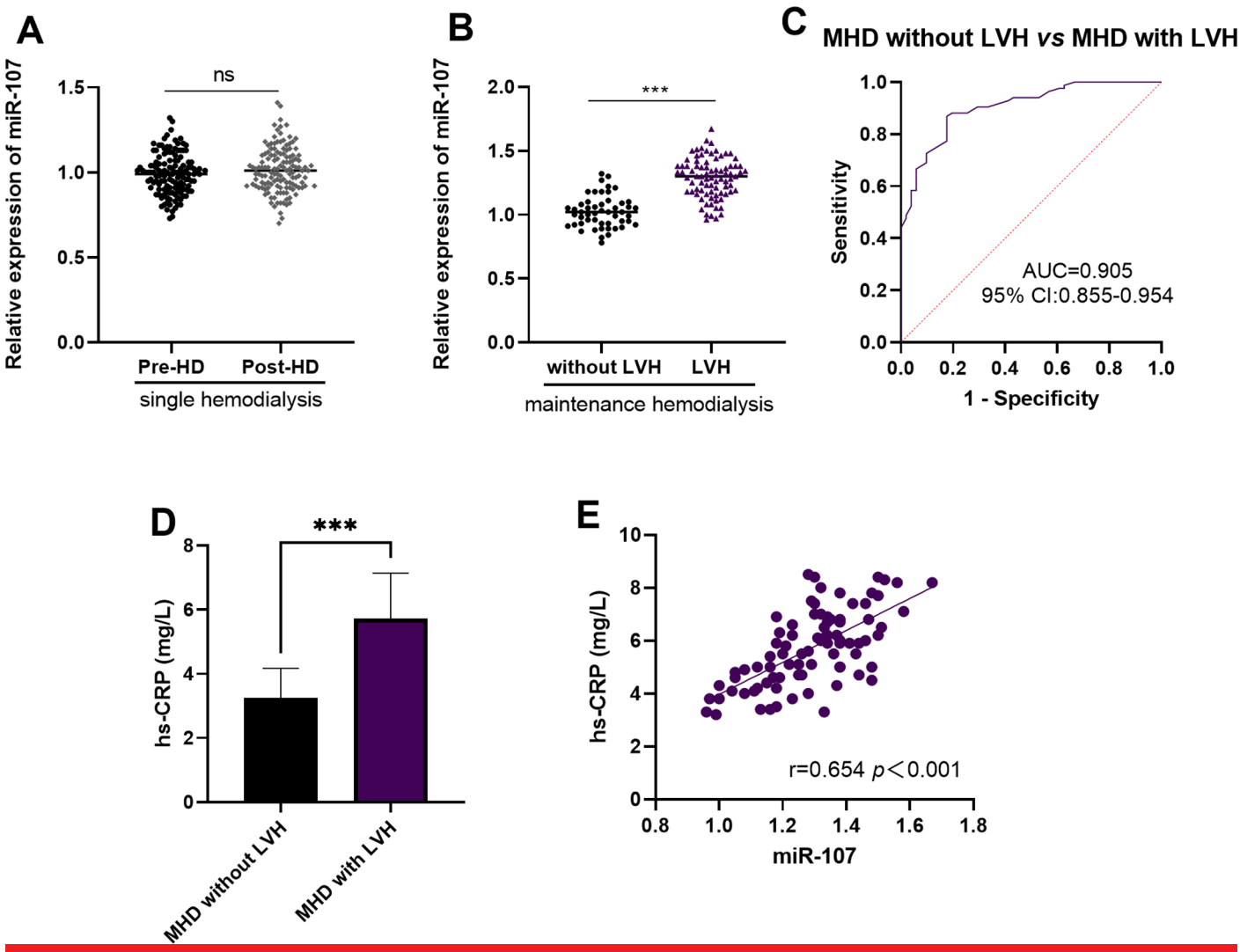

Figure 1. Expression and diagnostic significance of miR-107 in MHD with LVH patients. There was no significant difference in the expression of serum miR-107 before and after the first dialysis in the patients ($P > .05$) (A). The serum miR-107 level in the MHD with LVH group was higher than that in the MHD without LVH group ($P < .001$) (B). The ROC curve was used to evaluate the diagnostic value of miR-107 in MHD patients with LVH (C). The serum level of hs-CRP in MHD patients with LVH was significantly higher than that in the non-LVH group (D). A moderate positive correlation between the serum levels of miR-107 and hs-CRP in MHD patients with LVH ($r = 0.654$, $P < .001$) (E). ns, $P > .05$; *** $P < .001$.

than that in the non-LVH group (5.72 ± 1.42 mg/L vs. 2.87 ± 0.85 mg/L, $t = 12.94$, $P < .001$) (Figure 1D). Pearson correlation analysis showed a moderate positive correlation between the serum levels of miR-107 and hs-CRP in MHD patients with LVH ($r = 0.654$, 95% CI = 0.511-0.762, $P < .001$) (Figure 1E), suggesting that miR-107 may synergistically interact with the inflammatory response during the progression of LVH in MHD patients.

Correlation Between MiR-107 and Echocardiographic Features of Cardiac Hypertrophy in Maintenance Hemodialysis Patients

In the MHD with LVH group, IVST ($t = 15.45$), LVPWT ($t = 16.68$) and LVMI ($t = 15.04$) were significantly higher than those in the MHD without LVH group ($P < .001$) (Figure 2A-C). Furthermore, the results of the Pearson correlation analysis revealed a positive association between serum levels of miR-107 and IVST ($r = 0.619$, 95% CI = 0.466-0.736), LVPWT ($r = 0.662$, 95% CI = 0.521-0.767), and LVMI ($r = 0.528$, 95% CI = 0.354-0.667) in MHD patients with LVH ($P < .001$) (Figure 2D-F).

Analysis of Risk Factors for Cardiac Hypertrophy in Patients with Maintenance Hemodialysis

The findings from the logistic regression analysis revealed that miR-107 (odds ratio [OR] = 2.764, 95% CI = 1.229-6.219, $P = .014$), alongside hypertension (OR = 2.517, 95% CI = 1.097-5.777, $P = .029$) and diabetes (OR = 2.417, 95% CI = 1.031-5.664, $P = .042$) were identified as significant risk factors for MHD patients experiencing LVH (Table 3). The results of further multivariate logistic regression analysis showed that the OR of miR-107 was 2.459 (95% CI = 1.168-5.180, $P = .018$), suggesting that it is an independent risk factor for LVH (Table 4).

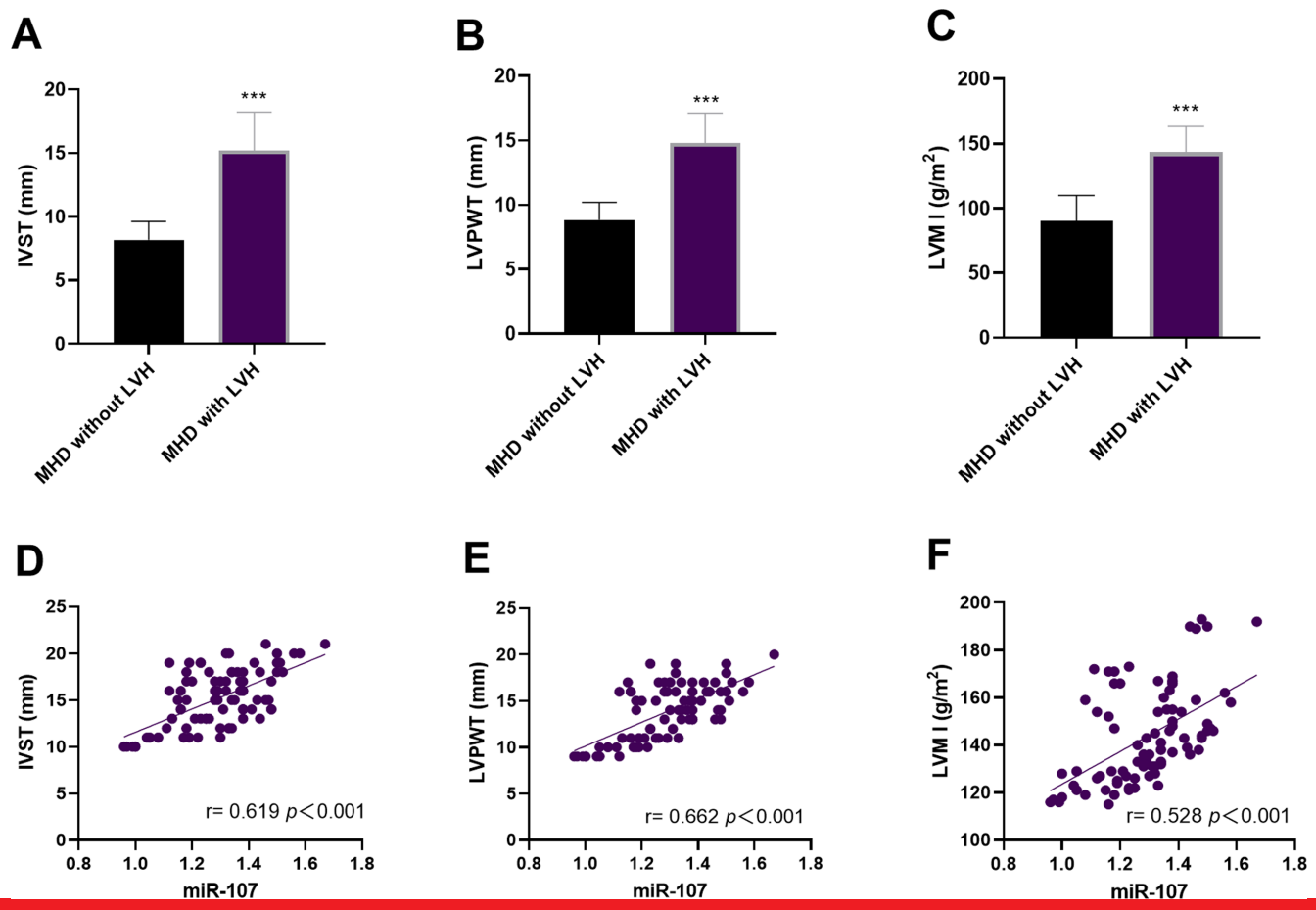

Figure 2. Correlation analysis of miR-107 with echocardiographic characteristics. In the MHD with LVH group, IVST, LVPWT and LVMI were significantly higher than those in the MHD without LVH group ($P < .001$) (A-C). The serum miR-107 level in MHD patients with LVH was positively correlated with IVST ($r = 0.619$), LVPWT ($r = 0.662$) and LVMI ($r = 0.528$) ($P < .001$) (D-F). *** $P < .001$

Table 3. Logistics Regression Analysis of the Risk Factors of Cardiac Hypertrophy in Chronic Hemodialysis Patient

		95% CI for HR		
Variables	**OR**	**Lower**	**Upper**	***P***
MiR-107	2.764	1.229	6.219	.014*
Age (years)	1.268	0.574	2.804	.557
Sex	1.827	0.786	4.248	.161
BMI	0.477	0.215	1.062	.070
Hypertension	2.517	1.097	5.777	.029*
Diabetes	2.417	1.031	5.664	.042*
MHD duration	1.291	0.584	2.851	.528
Hemoglobin	1.258	0.552	2.865	.585
Albumin	0.555	0.243	1.267	.162
PTH	1.476	0.655	3.324	.347
TC	1.591	0.703	3.600	.265
TG	1.190	0.542	2.613	.664
HDL-C	0.883	0.390	1.998	.765
LDL-C	1.320	0.595	2.927	.495

BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; HR, hazards ratio; LDL-C, low-density lipoprotein cholesterol; MHD, maintenance hemodialysis; OR, odds ratio; PTH, parathyroid hormone; TC, serum total cholesterol; TG, triglycerides.
*$P < .05$.

DISCUSSION

To address the hemodynamic stresses encountered during loading, the left ventricle adapts through physiological myocardial hypertrophy in the early stages, thereby preserving normal cardiac output in patients with MHD.[17] Left ventricular hypertrophy serves as a significant precursor to cardiovascular diseases, markedly influencing individuals' physical well-being and overall quality of life.[18] Emerging research increasingly elucidates the intricate relationship between miRNA and the development of cardiac hypertrophy in MHD patients.[19] Studies have shown that miR-217 promotes cardiac hypertrophy and dysfunction by targeting PTEN.[20] Concurrent findings suggest that miR-337-5p also plays a substantial role in the onset of cardiac hypertrophy.[21] Furthermore, elevated expression of miR-100-5p has been documented in the context of cardiac hypertrophy.[22] Similarly, the current results showed that the serum level of miR-107 was significantly upregulated in MHD patients with LVH, with a sensitivity of 86.9% and a specificity of 82.4% in diagnosing LVH. This finding is consistent with the previously reported elevated trend of miR-107 in hypertensive cardiomyopathy and diabetic cardiomyopathy,[23,24] suggesting that it may be involved in the common pathological processes of LVH caused by different etiologies.

Table 4. Multivariate Logistic Regression Analysis Results of Myocardial Hypertrophy in Patients Undergoing Chronic Hemodialysis

Variables	β	SE	Wald χ^2	*P*	OR	95% CI
MiR-107	0.900	0.380	5.608	.018*	2.459	1.168-5.180
Hypertension	0.914	0.394	5.387	.020*	2.494	1.153-5.394
Diabetes	0.733	0.398	3.397	.065	2.081	0.955-4.539

OR, odds ratio; SE, standard error.
*$P < .05$.

Chronic inflammation constitutes one of the core pathological features in patients undergoing MHD. C-reactive protein and particularly hs-CRP serve as a pivotal marker reflecting the state of chronic inflammation.[25] The present study revealed a significant positive correlation between miR-107 levels and hs-CRP in MHD patients with LVH, implying that inflammatory responses may represent a crucial mediating pathway through which miR-107 participates in the initiation and progression of LVH. This result supports miR-107 as a molecular marker for inflammation-cardiac remodeling coupling, providing a basis for the combined monitoring of miR-107 and hs-CRP in assessing the risk of LVH. Future research could target miR-107 to delve into its regulatory role in the inflammatory factor network, thereby providing novel targets and strategies for anti-inflammatory therapy of LVH in MHD patients.

Currently, the diagnosis of LVH relies on various techniques, including electrocardiogram (ECG), echocardiography, and cardiac magnetic resonance imaging (cMRI).[26] Left ventricular hypertrophy can be detected by echocardiography through the display of hypertrophy or other abnormalities typically associated with hypertrophic phenotypes.[27] The current study further establishes a close association between miR-107 and echocardiographic features in patients with MHD and LVH, identifying it as a critical risk factor for LVH in this patient population. These findings underscore the potential of miR-107 as a diagnostic or complementary diagnostic marker for MHD with LVH. Nonetheless, further investigation into its combined diagnostic efficacy is warranted.

Furthermore, it is important to underscore the significant impact of nursing interventions in mitigating complications and enhancing the therapeutic efficacy of HD throughout the MHD process.[28] End-stage renal disease is a critical pathological condition that arises when CKD progresses to an advanced stage, ultimately leading to partial or complete loss of renal function. This deterioration often results in the retention of metabolic waste products, as well as disturbances in water, electrolyte, and acid-base balance.[29] Maintenance hemodialysis has emerged as a widely adopted therapeutic approach for managing ESRD, effectively improving patients' quality of life and extending their longevity.[30] Additionally, the protracted nature of chronic renal failure leaves patients susceptible to negative emotional states such as anxiety and depression, which can adversely influence treatment outcomes.[31] Consequently, the implementation of effective and standardized nursing measures during HD for patients with chronic renal failure is paramount. The findings from this study indicate that, under targeted nursing interventions, the incidence of LVH was observed to be 62.2%. Previous studies have established that LVH is notably prevalent among patients with ESRD, with roughly 75% of MHD patients being affected.[32,33] Although the current data suggest a reduction in incidence compared to earlier research, further validation is required to substantiate this specific effect.

This investigation was conducted as a retrospective clinical study. However, it did not delve into the molecular mechanisms through which serum miR-107 influences cardiac hypertrophy and facilitates disease progression. Consequently, further in-depth research is warranted in this area. Additionally, the establishment of multi-center and large-scale studies is essential for both internal and external validation, which will ultimately enhance the predictive performance and clinical applicability of the model.

CONCLUSION

Serum miR-107 may have significant potential in diagnosing cardiac hypertrophy in MHD patients and is a potential biological indicator for cardiac hypertrophy in MHD patients.

Ethics Committee Approval: This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of The First Affiliated Hospital of Guizhou University of Traditional Chinese Medicine (Date: June 8, 2022; No. 20220101).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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Declaration of Interests: The authors have no conflicts of interest to declare.

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