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SHORT COMMUNICATION

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Circulating microRNAs as early molecular predictors of cardiac remodeling in pre-hypertensive individuals: A biotech perspective

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ABSTRACT

Cardiac remodeling is a dynamic and progressive process characterized by structural and molecular alterations in the myocardium, often occurring silently in the early stages of hypertension. Early detection remains a major clinical challenge, as conventional imaging and biochemical markers typically identify changes only after significant damage has occurred. Emerging evidence from molecular cardiology highlights circulating microRNAs **(miRNAs)**, notably **miR-21**, associated with myocardial fibrosis, and **miR-133a**, linked to cardiomyocyte hypertrophy, as promising early biomarkers of subclinical cardiac remodeling. This short communication presents findings from a focused observational study evaluating plasma levels of these miRNAs in pre-hypertensive individuals. Results demonstrated a consistent trend of **elevated miR-21** and **suppressed miR-133a** expression compared to normotensive controls, suggesting early molecular shifts in cardiac homeostasis. These findings underscore the potential for integrating microRNA-based diagnostics into routine screening, offering a novel, non-invasive tool for personalized risk assessment and early intervention in cardiovascular care.

KEYWORDS

Cardiac remodeling; microRNAs (miRNAs); miR-21; miR-133a; Pre-hypertension

ARTICLE HISTORY

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Introduction

Molecular cardiology is a rapidly advancing field that integrates molecular biology, genomics, and biotechnology to unravel the intricate mechanisms underlying cardiovascular diseases. Unlike traditional cardiology, which focuses primarily on anatomical and physiological abnormalities, molecular cardiology seeks to identify disease at its earliest stages, often before structural or symptomatic manifestations arise. This approach allows for more accurate risk stratification and the potential for early, personalized intervention [1]. As cardiovascular disease remains the leading cause of global mortality, innovations in molecular diagnostics are critical for improving long-term outcomes.

One of the earliest manifestations of chronic cardiovascular stress is cardiac remodeling, a complex process involving changes in myocardial structure, cellular composition, and gene expression. This remodeling can be initiated by prolonged exposure to elevated blood pressure, even in its pre-hypertensive phase. Alarmingly, many of these changes occur silently in young or otherwise healthy individuals, escaping detection by conventional imaging techniques or routine blood tests [2]. By the time symptoms or visible changes appear, significant and often irreversible damage may have already taken place.

Recent advancements in biotechnology have led to the discovery of **circulating microRNAs (miRNAs)** as promising biomarkers for early cardiac dysfunction [3]. These small, non-coding RNA molecules regulate gene expression and play vital roles in key cardiac pathways, including hypertrophy, apoptosis, and fibrosis. In particular, **miR-21**, associated with fibrotic remodeling, and **miR-133a**, known for its role in suppressing hypertrophy, have shown potential as non-invasive molecular indicators of early myocardial stress [4]. Their detection in peripheral blood offers a practical and scalable approach to identifying individuals at risk for cardiac remodeling before clinical symptoms emerge. This communication explores the potential of these biomarkers in pre-hypertensive individuals, highlighting their relevance in the future of personalized cardiovascular care [5].

Methods & Results

This short communication investigates whether select circulating microRNAs can be early biomarkers for cardiac remodeling in individuals with borderline hypertension. Drawing from molecular cardiology literature and known gene regulatory roles in myocardial tissues, two microRNAs were chosen: miR-21, associated with pro-fibrotic signaling, and miR-133a, known to suppress hypertrophic processes [6].

Participant selection and sample preparation

A pilot sample of 20 participants was divided into two groups. Group A (Pre-hypertensive) included 10 adults aged 25–35 years with resting systolic blood pressure between 125–139 mmHg and diastolic between 80–89 mmHg, with no history of cardiovascular disease. Group B (Normotensive controls) included 10 age- and gender-matched healthy individuals. Participants with any comorbidities or those on antihypertensive medication were excluded. After obtaining written informed consent, 5 mL of peripheral blood was collected from each participant into EDTA tubes. Plasma was isolated via centrifugation at 3000 rpm for 10 minutes and stored at –80°C [7].

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RNA extraction and quantification

Total RNA, including small RNAs, was extracted using the **miRNeasy Serum/Plasma Kit (Qiagen)**. RNA quality and concentration were assessed using a NanoDrop spectrophotometer. Expression levels of **miR-21** and **miR-133a** were quantified using **TaqMan qRT-PCR** assays with **U6 snRNA** as the internal control. All reactions were conducted in triplicate. Expression levels were calculated using the **2^-ΔΔCt method** to compare relative expression between the pre-hypertensive and normotensive groups [8].

Findings

The analysis revealed significant expression differences between the two groups. In pre-hypertensive individuals (Group A), miR-21 was upregulated by approximately 2.3-fold, while miR-133a was downregulated to 0.6-fold compared to the normotensive controls (Group B), in which both markers were normalized to baseline expression of 1.0. These changes suggest early molecular alterations reflective of cardiac remodeling processes, despite the absence of any clinical symptoms or structural abnormalities detectable through imaging (Table 1) [7].

Table 1. Relative Expression of Circulating microRNAs in Study Participants.

Group	miR-21 (Fold Change)	miR-133a (Fold Change)
Normotensive (n = 10)	1.0 (baseline)	1.0 (baseline)
Pre-hypertensive (n = 10)	↑ 2.3-fold	↓ 0.6-fold

Expression values normalized to U6 snRNA using the 2^-ΔΔCt method.

These findings, while preliminary, demonstrate the potential of circulating microRNAs as non-invasive, biotech-based molecular tools for detecting subclinical cardiac remodeling. The expression profiles of miR-21 and miR-133a provide an early molecular signature of pathological change, long before conventional diagnostics indicate cardiovascular risk [9].

Discussion & Future Application

The results of this pilot investigation underscore the critical role of molecular markers particularly circulating microRNAs as early predictors of cardiac remodeling, even before structural abnormalities or clinical symptoms emerge [10]. Unlike imaging modalities or functional cardiac assessments, which often detect changes only after significant physiological damage has occurred, microRNAs such as miR-21 and miR-133a offer insight into the initial stages of myocardial stress and remodeling at the gene expression level [11].

Compared to traditional cardiac biomarkers like NT-proBNP, which primarily reflect volume overload or overt cardiac dysfunction, microRNA profiling detects subtler, cell-specific processes such as fibrosis and hypertrophy regulation [12]. Similarly, ECG and echocardiography, while useful for identifying electrical or anatomical abnormalities, may appear normal in pre-hypertensive individuals despite ongoing molecular-level changes. This positions microRNA analysis as a more sensitive and proactive tool for early cardiovascular risk assessment [13].

From a translational standpoint, the integration of microRNA testing into point-of-care diagnostics could redefine preventive cardiology. With advancements in microfluidics and biosensor platforms, it is now technically feasible to incorporate nucleic acid detection into portable, rapid diagnostic kits [14]. Such devices could enable early screening of at-risk populations including young adults with a family history of hypertension at community health centers, student clinics, or even in workplace wellness programs.

In terms of cost-effectiveness, microRNA-based screening holds promise due to its minimal sample requirements (a few microliters of plasma), rapid turnaround time, and declining costs of molecular assays. Compared to repeated imaging tests or late-stage hospitalizations for cardiovascular events, early detection via blood-based biomarkers is potentially more scalable and economically sustainable, particularly in primary care settings [15].

In the future, microRNA panels could be combined with AI-powered decision tools, wearable health monitors, and electronic health records to create personalized cardiovascular risk dashboards. This integrative approach not only enhances early detection but also aligns with the growing emphasis on precision medicine and biotech-driven healthcare innovations [16].

Conclusions

Circulating microRNAs such as miR-21 and miR-133a hold strong potential as early molecular indicators of cardiac remodeling, particularly in asymptomatic or pre-hypertensive individuals. Their ability to reflect cellular-level changes before structural or functional damage becomes apparent offers a valuable window for early intervention. When incorporated into biotech-driven diagnostic platforms, microRNA profiling can empower clinicians to identify at-risk individuals far earlier than with traditional methods like ECG or echocardiography. This shift from reactive to preventive care may significantly reduce the long-term burden of cardiovascular disease. As detection technologies become more accessible and cost-efficient, integrating microRNA-based tools into routine screening protocols could transform the future of precision cardiology.

Disclosure Statement

The authors declare that they have no competing interests.

References

1. Nayor M, Brown KJ, Vasan RS. The molecular basis of predicting atherosclerotic cardiovascular disease risk. Circ Res. 2021;128(2): 287-303. https://doi.org/10.1161/CIRCRESAHA.120.315890
2. Antropova ON, Silkina SB, Polyakova IG, Perevozchikova TV. Association of hemodynamic parameters and cardiovascular risk factors with cardiac remodeling in young patients with prehypertension and hypertension. Russ J Cardiol. 2020;25(6):3797. https://doi.org/10.15829/1560-4071-2020-3797
3. Zhou SS, Jin JP, Wang JQ, Zhang ZG, Freedman JH, Zheng Y, et al. miRNAS in cardiovascular diseases: potential biomarkers, therapeutic targets and challenges. Acta Pharmacol Sin. 2018;39(7):1073-1084. https://doi.org/10.1038/aps.2018.30
4. Wang J, Liew OW, Richards AM, Chen YT. Overview of microRNAs in cardiac hypertrophy, fibrosis, and apoptosis. Int J Mol Sci.

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https://doi.org/10.61577/ijcri.2024.1000025

2016;17(5):749. https://doi.org/10.3390/ijms17050749
5. Shah RV, Rong J, Larson MG, Yeri A, Ziegler O, Tanriverdi K, et al. Associations of circulating extracellular RNAs with myocardial remodeling and heart failure. JAMA Cardiol. 2018;3(9):871-876. https://doi.org/10.1001/jamacardio.2018.2371
6. Wehbe N, Nasser SA, Pintus G, Badran A, Eid AH, Baydoun E. MicroRNAs in cardiac hypertrophy. Int J Mol Sci. 2019;20(19):4714. https://doi.org/10.3390/ijms20194714
7. Matshazi DM, Weale CJ, Erasmus RT, Kengne AP, Davids SF, Raghubeer S, et al. MicroRNA profiles in normotensive and hypertensive south African individuals. Front Cardiovasc Med. 2021;8:645541. https://doi.org/10.3389/fcvm.2021.645541
8. Hijmans JG, Diehl KJ, Bammert TD, Kavlich PJ, Lincenberg GM, Greiner JJ, et al. Association between hypertension and circulating vascular-related microRNAs. J Hum Hypertens. 2018;32(6): 440-447. https://doi.org/10.1038/s41371-018-0061-2
9. De Gonzalo-Calvo D, Iglesias-Gutierrez E, Llorente-Cortes V. Epigenetic biomarkers and cardiovascular disease: circulating microRNAs. Rev Esp Cardiol. 2017;70(9):763-769. https://doi.org/10.1016/j.rec.2017.05.013
10. D'Alessandra Y, Chiesa M, Carena MC, Beltrami AP, Rizzo P, Buzzetti M, et al. Differential role of circulating microRNAs to track progression and pre-symptomatic stage of chronic heart failure: a pilot study. Biomedicines. 2020;8(12):597. https://doi.org/10.3390/biomedicines8120597
11. Chen C, Ponnusamy M, Liu C, Gao J, Wang K, Li P. MicroRNA as a therapeutic target in cardiac remodeling. Biomed Res Int. 2017;2017(1):1278436. https://doi.org/10.1155/2017/1278436
12. Wong LL, Zou R, Zhou L, Lim JY, Phua DC, Liu C, et al. Combining circulating microRNA and NT-proBNP to detect and categorize heart failure subtypes. J Am Coll Cardiol. 2019;73(11):1300-1313. Available at https://www.jacc.org/doi/abs/10.1016/j.jacc.2018.11.060
13. Searles CD. MicroRNAs and cardiovascular disease risk. Curr Cardiol Rep. 2024;26(2):51-60. https://doi.org/10.1007/s11886-023-02014-1
14. Cheong JK, Tang YC, Zhou L, Cheng H, Too HP. Advances in quantifying circulatory microRNA for early disease detection. Curr Opin Biotechnol. 2022;74:256-262. https://doi.org/10.1016/j.copbio.2021.12.007
15. Felekkis K, Papaneophytou C. Challenges in using circulating micro-RNAs as biomarkers for cardiovascular diseases. Int J Mol Sci. 2020;21(2):561. https://doi.org/10.3390/ijms21020561
16. Haq IU, Haq I, Xu B. Artificial intelligence in personalized cardiovascular medicine and cardiovascular imaging. Cardiovasc Diagn The. 2021;11(3):911. https://doi.org/10.21037/cdt.2020.03.09

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