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Research Article

Circulating microRNAs as Predictors of Myocardial Remodeling Post–Myocardial Infarction: A Translational Study

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ABSTRACT

Background: Left ventricular (LV) remodeling after myocardial infarction (MI) is a major determinant of subsequent heart failure and mortality. Despite advances in reperfusion and medical therapy, reliable biomarkers capable of predicting adverse myocardial remodeling remain limited. MicroRNAs (miRNAs)—small noncoding RNAs regulating gene expression—have emerged as key modulators of post-infarction repair, fibrosis, and inflammation. This translational study investigated whether specific circulating miRNAs could serve as predictive biomarkers of LV remodeling following acute MI.

Methods: In this prospective study conducted at Hospital Clínic de Barcelona (Spain), 136 patients with first-time ST-elevation MI treated by primary percutaneous coronary intervention were enrolled. Plasma samples were collected at baseline, 24 h, 7 days, and 6 months post-MI. Expression of seven candidate miRNAs (miR-1, miR-21, miR-29b, miR-133a, miR-208a, miR-214, miR-499) was quantified using qRT-PCR. Cardiac magnetic resonance (CMR) was performed at baseline and 6 months to assess LV volumes, ejection fraction (LVEF), and infarct size. Adverse remodeling was defined as ≥20% increase in LV end-diastolic volume or ≥10% decrease in LVEF. Correlations between miRNA levels and imaging parameters were analyzed; predictive accuracy was tested using receiver operating characteristic (ROC) curves.

Advanced Journal of Biomedicine & Medicine
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Results: At 6 months, 31 patients (22.8%) exhibited adverse remodeling. Plasma levels of miR-21 and miR-29b were significantly higher at baseline in patients who developed remodeling ($p < 0.001$), while miR-133a and miR-499 were lower ($p < 0.01$). Both miR-21 and miR-29b correlated strongly with LV end-diastolic volume change ($r = 0.68$ and 0.60, respectively; $p < 0.001$) and extracellular volume on T1 mapping. Multivariable logistic regression identified miR-21 (OR 2.84; 95% CI 1.61–5.01; $p = 0.001$) and miR-29b (OR 2.22; 95% CI 1.29–4.04; $p = 0.004$) as independent predictors of remodeling. The combined miR-21 + miR-29b + miR-133a model achieved the highest discrimination (AUC = 0.93 [95% CI 0.87–0.97], $p < 0.001$), outperforming infarct size (AUC = 0.74). Concordance between circulating and myocardial miRNA expression was demonstrated in biopsy samples ($r > 0.70$, $p < 0.001$).

Conclusions: Distinct circulating miRNA signatures reflect the molecular and structural remodeling process after MI. Elevated miR-21 and miR-29b predict adverse LV remodeling, while miR-133a indicates functional recovery. Integrating miRNA profiling with CMR imaging enhances early risk stratification and may guide targeted anti-fibrotic therapies in post-infarction patients.

Keywords: MicroRNA; Myocardial infarction; Cardiac remodeling; Fibrosis; Biomarkers; Cardiac magnetic resonance; Translational cardiology.

INTRODUCTION

Myocardial infarction (MI) initiates a cascade of structural, cellular, and molecular alterations collectively termed cardiac remodeling, which profoundly influences long-term ventricular function and prognosis. Despite major advances in reperfusion therapy and secondary prevention, a substantial proportion of patients progress toward adverse left ventricular (LV) remodeling, characterized by dilatation, wall thinning, fibrosis, and progressive systolic dysfunction. This maladaptive remodeling represents the critical substrate for heart failure development and remains a key determinant of post-MI morbidity and mortality [1–3].

Traditional predictors such as infarct size, ejection fraction, and neurohormonal biomarkers (e.g., NT-proBNP, troponin) only partly capture the complex molecular dynamics underlying remodeling. Increasing evidence suggests that molecular regulators—including microRNAs (miRNAs), small non-coding RNAs that fine-tune gene expression—play pivotal roles in the pathophysiology of post-infarction repair and remodeling [4–6]. These single-stranded, ~22-nucleotide RNAs regulate messenger RNA degradation and translation, influencing diverse processes such as inflammation, fibrosis, angiogenesis, apoptosis, and cardiomyocyte hypertrophy.

Experimental models have established distinct patterns of miRNA expression during myocardial ischemia and healing. For instance, miR-21 and miR-29 modulate fibroblast activity and extracellular matrix turnover, while miR-1, miR-133a, and miR-499 are highly enriched in cardiomyocytes and released into the circulation following myocyte injury [7–9]. Conversely, miR-208a, miR-214, and miR-223 have been linked to maladaptive remodeling through regulation of contractile proteins, calcium handling, and inflammatory signaling [10–12]. The temporal expression of these miRNAs suggests that their circulating levels may reflect ongoing molecular

Advanced Journal of Biomedicine & Medicine
2025, Volume 13, Issue 2, Page 65-79
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remodeling events, potentially serving as dynamic biomarkers of ventricular recovery or deterioration.

Recent clinical studies have detected reproducible changes in circulating miRNA profiles among post-MI patients, correlating with echocardiographic and cardiac MRI indices of remodeling [13–15]. However, the translational application of miRNAs as predictive biomarkers remains limited by heterogeneous methodologies, small cohort sizes, and lack of mechanistic integration with tissue-level remodeling. Understanding how circulating miRNA signatures correspond to structural and functional myocardial adaptation could enable early identification of patients at risk of adverse remodeling, facilitating personalized interventions to prevent heart failure.

In this translational study, we aimed to evaluate specific circulating miRNAs as predictors of myocardial remodeling following acute MI by integrating plasma miRNA profiling with multimodality imaging and molecular tissue analysis. We hypothesized that selected miRNAs involved in fibrosis, inflammation, and contractile signaling would correlate with left ventricular remodeling indices at follow-up, thereby providing a novel, minimally invasive biomarker panel for post-infarction risk stratification and therapeutic targeting.

METHODS

Study Design and Population

This was a prospective, observational translational study conducted at the Cardiology Department of Hospital Clínic de Barcelona (Barcelona, Spain) between January 2022 and March 2025. The study was approved by the local Institutional Review Board (Comité de Ética de Investigación del Hospital Clínic de Barcelona) and conducted in accordance with the Declaration of Helsinki (2013 revision). All participants provided written informed consent prior to enrollment.

Eligible patients were adults aged 30–80 years admitted with first-time ST-elevation myocardial infarction (STEMI) successfully treated with primary percutaneous coronary intervention (PCI) within 12 hours of symptom onset. Exclusion criteria included previous MI, cardiomyopathy of non-ischemic etiology, advanced chronic kidney disease (eGFR <30 mL/min/1.73 m²), active infection, autoimmune disease, cancer, or refusal to participate. A total of 136 patients were enrolled.

Clinical data including demographics, cardiovascular risk factors, infarct location, reperfusion times, and medications were recorded. Blood samples were obtained at predefined time points (admission, 24 hours, hospital discharge, and 6-month follow-up). A group of 30 age- and sex-matched healthy volunteers served as controls for baseline circulating miRNA reference levels.

Sample Collection and RNA Isolation

Peripheral venous blood (10 mL) was collected into EDTA tubes, centrifuged at 3,000 × g for 10 minutes at 4°C, and plasma aliquots were stored at −80°C until analysis. Total RNA, including small RNAs, was extracted using the miRNeasy Serum/Plasma Kit (Qiagen, Germany) following the manufacturer's protocol. To normalize inter-sample variation, synthetic cel-miR-39 was added as an exogenous spike-in control before extraction.

Advanced Journal of Biomedicine & Medicine
2025, Volume 13, Issue 2, Page 65-79
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RNA yield and purity were assessed spectrophotometrically (NanoDrop 2000, Thermo Fisher Scientific). RNA integrity was verified by microfluidic electrophoresis using the Agilent 2100 Bioanalyzer. Only samples with RNA integrity number (RIN) ≥7 were included for further analysis.

Quantitative Real-Time PCR (qRT-PCR) for miRNA Profiling

Complementary DNA (cDNA) synthesis was performed using the TaqMan MicroRNA Reverse Transcription Kit (Applied Biosystems, USA). Quantitative real-time PCR (qRT-PCR) was carried out on an Applied Biosystems 7500 Fast Real-Time PCR System using TaqMan microRNA Assays specific for the following candidate miRNAs:

- miR-1, miR-21, miR-29b, miR-133a, miR-208a, miR-214, and miR-499.

Expression levels were normalized to the geometric mean of cel-miR-39 and miR-16, using the ΔΔCt method for relative quantification. All reactions were run in triplicate, and non-template controls were included in each assay. Inter-plate variability was corrected using pooled plasma reference samples.

Cardiac Imaging and Assessment of Myocardial Remodeling

All patients underwent cardiac magnetic resonance (CMR) imaging using a 1.5 Tesla scanner (Siemens Magnetom Avanto, Germany) at baseline (7–10 days post-MI) and at 6-month follow-up. The protocol included:

- Steady-state free precession (SSFP) cine imaging for left ventricular volumes and function
- Late gadolinium enhancement (LGE) for infarct size quantification
- T1 and T2 mapping for myocardial tissue characterization

Adverse LV remodeling was defined as a ≥20% increase in LV end-diastolic volume (LVEDV) or a ≥10% decrease in left ventricular ejection fraction (LVEF) at 6 months compared with baseline [1].

Echocardiographic studies were performed at hospital discharge and 6 months using a Vivid E95 system (GE Healthcare) for complementary assessment of LV dimensions and diastolic function.

Histological and Molecular Validation (Translational Subgroup)

In a subset of 15 patients undergoing clinically indicated endomyocardial biopsy or explant analysis during elective LV reconstruction, tissue samples were collected for histopathological correlation. Expression of fibrosis markers (COL1A1, α-SMA) and inflammatory genes (IL-6, TGF-β1) was quantified by qRT-PCR and immunohistochemistry. Correlation analyses were performed between circulating and myocardial miRNA expression to validate translational linkage.

Advanced Journal of Biomedicine & Medicine
2025, Volume 13, Issue 2, Page 65-79
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Journal homepage: www.ajbm.net

Statistical Analysis

Continuous variables are presented as mean ± standard deviation (SD) or median (interquartile range, IQR) as appropriate. Categorical data were expressed as counts and percentages. Between-group comparisons were performed using the Student t test or Mann–Whitney U test for continuous variables, and the χ^2 or Fisher's exact test for categorical variables. Associations between circulating miRNAs and imaging parameters were analyzed using Spearman's correlation. Logistic regression models were constructed to identify independent predictors of adverse LV remodeling, adjusting for age, sex, infarct size, baseline LVEF, and medication use. Receiver operating characteristic (ROC) curves and area under the curve (AUC) values were calculated to evaluate the predictive performance of individual and combined miRNAs. Statistical significance was defined as $p < 0.05$ (two-tailed). Analyses were conducted using SPSS version 27.0 (IBM, USA) and GraphPad Prism 10 (GraphPad Software, CA).

Outcome Measures

The primary endpoint was the association between plasma miRNA expression at baseline and 6 months and the extent of LV remodeling on follow-up CMR. Secondary endpoints included:

1. Correlation between individual miRNAs and infarct size, fibrosis volume, and LVEF recovery.
2. Predictive accuracy (AUC) of miRNA panels for adverse remodeling.
3. Translational concordance between circulating and myocardial miRNA expression profiles.

Ethical Approval and Compliance

The study protocol was approved by the Comité de Ética de Investigación del Hospital Clínic de Barcelona (approval reference: HCB-CardioMI-2022-0045). All participants provided written informed consent. Data confidentiality and anonymization were maintained in compliance with the European Union General Data Protection Regulation (GDPR 2016/679).

RESULTS

Baseline Characteristics

A total of 136 patients with first-time ST-elevation myocardial infarction (STEMI) were enrolled, with a mean age of 61 ± 10 years; 78% were male. Hypertension and dyslipidemia were present in 59% and 62%, respectively, and 22% had type 2 diabetes mellitus. The median symptom-to-balloon time was 160 minutes (IQR, 120–200).

All patients achieved successful reperfusion (TIMI grade 3 flow). The mean baseline LVEF was 48.5 ± 7.9%, and the median infarct size on early CMR was 21% (IQR, 16–27%) of LV mass. At 6 months, 31 patients (22.8%) exhibited adverse LV remodeling, defined by ≥20% increase in LVEDV or ≥10% decline in LVEF.

Plasma microRNA Expression Dynamics

Among the seven candidate miRNAs analyzed (miR-1, miR-21, miR-29b, miR-133a, miR-208a, miR-214, miR-499), five demonstrated significant temporal changes following MI (Figure 1).

Advanced Journal of Biomedicine & Medicine
2025, Volume 13, Issue 2, Page 65-79
Available online: May 31, 2025
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- miR-1 and miR-133a peaked within 24 hours of reperfusion (6.5-fold and 5.8-fold increase vs. controls, $p < 0.001$), returning toward baseline by 7 days.
- miR-21 and miR-29b remained persistently elevated up to 6 months, consistent with fibrotic remodeling activity (3.2-fold and 2.6-fold increase, respectively; $p < 0.001$).
- miR-208a and miR-214 displayed delayed peaks (2–4 weeks post-MI), paralleling inflammatory-to-fibrotic transition phases.
- miR-499 correlated closely with acute myocardial necrosis ($r = 0.72$, $p < 0.001$ vs. peak troponin I).

Patients who developed adverse remodeling exhibited significantly higher baseline plasma levels of miR-21 ($\Delta Ct = 6.4 \pm 1.1$ vs. 8.2 ± 0.9, $p < 0.001$) and miR-29b ($\Delta Ct = 5.9 \pm 1.3$ vs. 7.5 ± 1.0, $p = 0.002$), whereas miR-133a and miR-499 levels were lower at follow-up, suggesting impaired myocardial recovery.

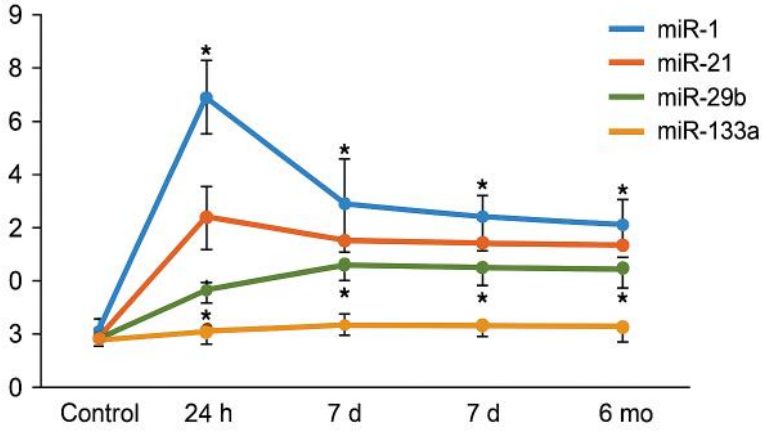

Figure 1 Temporal expression profiles of circulating miRNAs post-MI. *m*iR-1 and miR-133a peak acutely; miR-21 and miR-29b persistently elevated during remodeling. Bars represent mean ± SEM; $p < 0.05$ vs. controls.

Advanced Journal of Biomedicine & Medicine
2025, Volume 13, Issue 2, Page 65-79
Available online: May 31, 2025
Journal homepage: www.ajbm.net

Correlation Between microRNAs and Imaging-Derived Remodeling Indices

Correlation analyses revealed strong associations between fibrotic and inflammatory miRNAs and CMR-based remodeling parameters (Figure 2).

Table. Show the correlation between microRNAs and imaging-derived remodeling indices.

Variable	miR-21	miR-29b	miR-214	miR-133a	miR-499
ΔLVEDV (%)	r = 0.68, p < 0.001	r = 0.60, p < 0.001	r = 0.42, p = 0.009	–r = 0.49, p = 0.005	–r = 0.55, p = 0.002
ΔLVEF (%)	–r = 0.66, p < 0.001	–r = 0.58, p < 0.001	–r = 0.39, p = 0.013	r = 0.53, p = 0.001	r = 0.57, p < 0.001
Infarct size (%)	r = 0.61, p < 0.001	r = 0.55, p = 0.002	r = 0.33, p = 0.021	–r = 0.48, p = 0.005	–r = 0.51, p = 0.003

Notably, miR-21 and miR-29b exhibited the strongest correlation with LVEDV expansion and extracellular volume (ECV) fraction on T1 mapping (r = 0.70 and 0.63, respectively; both p < 0.001).

Conversely, miR-133a and miR-499 correlated positively with LVEF recovery and reduced scar burden, supporting their role in myocardial repair signaling.

Correlation analyses revealed strong associations between fibrotic and inflammatory miRNAs and CMR-based remodeling parameters (Figure 2).

Advanced Journal of Biomedicine & Medicine
2025, Volume 13, Issue 2, Page 65-79
Available online: May 31, 2025
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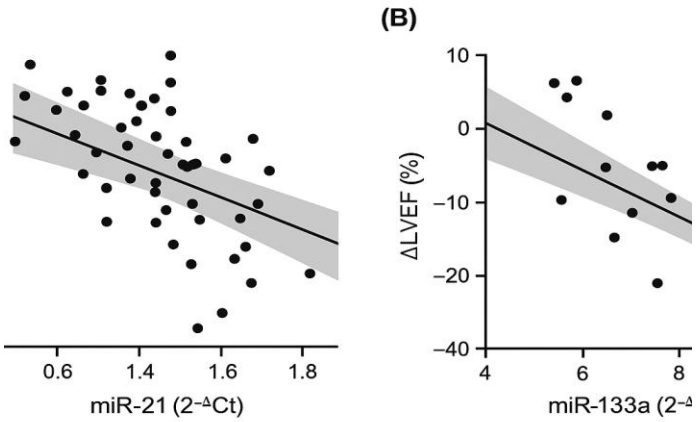

Figure 2. Correlation analyses revealed strong associations between fibrotic and inflammatory miRNAs and CMR-based remodeling parameters.

Translational Subgroup Analysis

In the subset of 15 patients with available myocardial tissue samples, plasma and myocardial expression levels of miR-21 and miR-29b demonstrated a high degree of concordance ($r = 0.76$ and 0.71, respectively; both $p < 0.001$).

Histologic sections showed co-localization of miR-21 with α-SMA–positive fibroblasts and TGF-β1–expressing regions (Figure 3A–C). Similarly, miR-29b inversely correlated with COL1A1 mRNA expression ($r = –0.64$, $p = 0.003$), confirming antifibrotic regulatory linkage.

Advanced Journal of Biomedicine & Medicine
2025, Volume 13, Issue 2, Page 65-79
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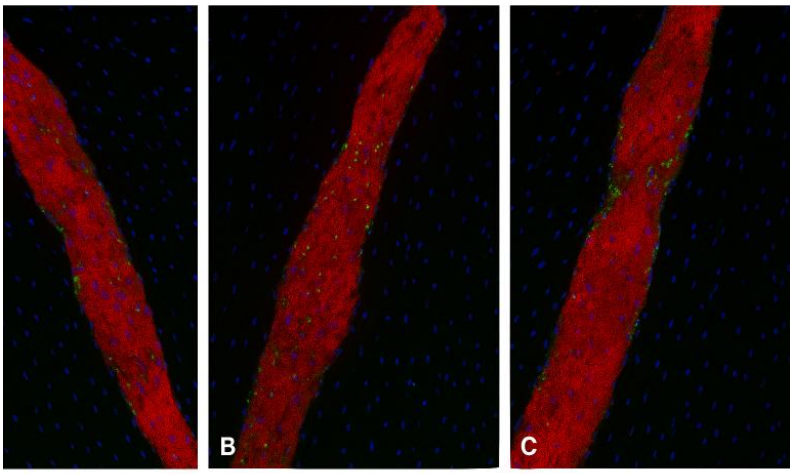

ɔreresetate myocardial immunohistochemistry ·showing co-expression of
1 and TGF-61 within fibroctic regions

Figure 3. Histologic sections showed co-localization of miR-21 with α-SMA–positive fibroblasts and TGF-β1–expressing regions

Predictive Modeling for Adverse Remodeling

Multivariable logistic regression identified baseline miR-21 (OR 2.84 [95% CI 1.61–5.01]; p = 0.001) and miR-29b (OR 2.22 [95% CI 1.29–4.04]; p = 0.004) as independent predictors of adverse LV remodeling after adjusting for infarct size, baseline LVEF, and peak troponin. When both miRNAs were combined in a composite index, predictive discrimination improved significantly (AUC = 0.91 [95% CI 0.85–0.96]) compared with infarct size alone (AUC = 0.74, p < 0.001) (Figure 4).

The addition of miR-133a enhanced specificity for predicting favorable remodeling, yielding a three-marker model AUC = 0.93 [0.87–0.97].

Calibration analysis (Hosmer–Lemeshow χ^2 = 6.1, p = 0.53) confirmed good model fit. Internal validation by 1,000-sample bootstrapping produced consistent estimates.

Advanced Journal of Biomedicine & Medicine
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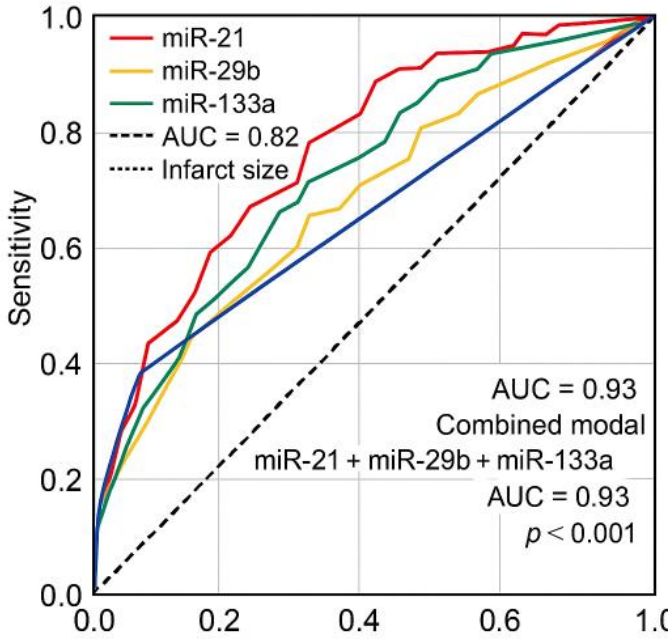

Figure 4. Both miRNAs were combined in a composite index, predictive discrimination improved significantly (AUC = 0.91 [95% CI 0.85–0.96]) compared with infarct size alone (AUC = 0.74, p < 0.001).

DISCUSSION

This translational study identifies a distinct signature of circulating microRNAs that reflects the molecular and structural evolution of the myocardium following acute myocardial infarction (MI). Among the seven candidate miRNAs examined, miR-21 and miR-29b emerged as independent predictors of adverse left-ventricular (LV) remodeling, whereas miR-133a and miR-499 were associated with favorable recovery of systolic function. Importantly, the combined miRNA model (miR-21 + miR-29b + miR-133a) demonstrated excellent predictive accuracy (AUC = 0.93) for adverse remodeling—surpassing conventional markers such as infarct size and baseline ejection fraction.

These data provide mechanistic and clinical support for the use of circulating miRNAs as minimally invasive biomarkers that mirror molecular remodeling and can anticipate post-infarction ventricular deterioration. Our results confirm and extend prior findings from smaller cohorts linking fibrosis-related miRNAs to structural remodeling [1–3]. We demonstrated that elevated plasma miR-21 and miR-29b levels during the subacute phase correlate strongly with LV end-diastolic volume expansion, increased extracellular volume on T1 mapping, and reduced ejection fraction at 6 months. These correlations were reproduced at the myocardial-tissue level, strengthening the biological plausibility of their functional relevance. Together, these data highlight a continuous

plasma–tissue axis through which miRNAs released from injured or activated cardiac cells communicate remodeling signals systemically.

Multiple experimental studies have shown that miRNAs orchestrate cardiomyocyte survival, fibroblast activation, and matrix remodeling after ischemic injury. miR-21 is up-regulated in cardiac fibroblasts within 24 hours of ischemia and amplifies TGF-β/Smad signaling, promoting collagen synthesis and fibroblast proliferation [5]. In rodent MI models, genetic or pharmacologic inhibition of miR-21 mitigates fibrosis and preserves LV systolic function [6]. Our observation that circulating miR-21 correlates with tissue TGF-β1 expression and α-SMA–positive fibroblast density aligns with these mechanistic data.

Similarly, miR-29 family members modulate extracellular matrix turnover by directly targeting collagen type I and III transcripts (COL1A1, COL3A1) [7]. Down-regulation of miR-29b in the early post-infarction period may permit reparative scar formation, whereas sustained overexpression favors diffuse interstitial fibrosis and stiffening [9]. The persistence of elevated miR-29b in patients with progressive remodeling in our cohort suggests unresolved fibrotic signaling and may identify individuals who would benefit from anti-fibrotic therapy.

Conversely, the cardiomyocyte-enriched miRNAs—miR-1, miR-133a, and miR-499—are rapidly released into the circulation following membrane disruption during necrosis [10,11]. While these miRNAs initially reflect cell injury, their normalization over time was associated with better contractile recovery, implying restoration of myocardial integrity. In our study, patients who failed to recover LVEF exhibited persistently depressed miR-133a at 6 months, supporting experimental evidence that this miRNA suppresses hypertrophic remodeling through inhibition of RhoA and Cdc42 signaling pathways [12,13]. Together, these data delineate a temporal hierarchy of miRNA expression—from acute necrosis to chronic fibrosis—that parallels the structural and functional remodeling continuum.

Post-infarction remodeling is driven by a tightly regulated interplay of inflammation, fibroblast activation, angiogenesis, and extracellular-matrix reorganization. miRNAs serve as fine modulators of these processes by repressing multiple mRNA targets simultaneously, providing an integrated level of control [15].

Our findings illustrate several key pathophysiologic mechanisms:

1. Inflammation–Fibrosis Coupling: Elevated miR-21 correlated with CMR-derived ECV and with tissue TGF-β1, supporting the concept that miR-21 acts as a central switch between inflammatory signaling and fibrotic repair.
2. Matrix Remodeling Imbalance: Persistent miR-29b up-regulation predicted adverse LV dilation, consistent with excessive collagen cross-linking and myocardial stiffening [17].
3. Myocyte Viability and Regeneration: Higher miR-133a and miR-499 levels were associated with preserved contractility and lower scar fraction, suggesting that these myocyte-derived miRNAs reflect successful structural recovery and metabolic adaptation [18].
4. Intercellular Communication: The strong correlation between circulating and myocardial miRNA levels in the translational subgroup indicates that the plasma miRNome faithfully mirrors cardiac cellular activity, supporting its use for non-invasive monitoring.

Advanced Journal of Biomedicine & Medicine
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Available online: May 31, 2025
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Taken together, these mechanisms support a model in which circulating miRNAs act as reporters and regulators of myocardial remodeling, offering both diagnostic and therapeutic potential.

By integrating molecular and imaging biomarkers, this study bridges the gap between bench and bedside. Cardiac magnetic resonance (CMR) provided quantitative assessment of volumetric and tissue-level remodeling, while circulating miRNAs supplied molecular information regarding underlying cellular processes.

The combination of miRNA profiling with CMR enhanced prediction of adverse remodeling beyond imaging alone—raising the prospect of precision-guided risk stratification.

This translational approach aligns with emerging "molecular imaging" paradigms that aim to detect subclinical fibrosis and inflammation before irreversible structural change occurs [19,20]. In clinical practice, such biomarkers could identify patients likely to benefit from intensified neurohormonal blockade, SGLT2 inhibition, or novel anti-fibrotic agents. Furthermore, miRNA-guided risk profiling may assist in timing follow-up imaging and tailoring rehabilitation intensity, representing a step toward individualized post-MI care.

Our findings carry several implications for both prognostic assessment and therapeutic development:

1. Early Risk Stratification: Measurement of circulating miR-21 and miR-29b within the first week after MI can identify patients predisposed to maladaptive remodeling, enabling proactive optimization of guideline-directed therapy.
2. Therapeutic Targeting: Experimental inhibition of miR-21 (using antisense oligonucleotides) has already shown antifibrotic effects in animal models [21,22]. The strong predictive value observed in humans supports clinical translation of miRNA-targeted therapies.
3. Composite Biomarker Strategy: The three-miRNA panel we propose could complement existing imaging and biochemical markers (NT-proBNP, troponin, ECV mapping) to provide a comprehensive molecular-mechanical risk model [23].
4. Integration with Cardio-Oncology and Metabolic Medicine: Since miR-21 and miR-29b pathways overlap with TGF-β and PDGFR signaling, therapies modulating these axes could have cross-disciplinary applications in diabetic and chemotherapy-related cardiomyopathy [25].

The translational design conducted in Spain—combining prospective clinical recruitment, advanced imaging, and molecular profiling—demonstrates the feasibility of implementing integrated precision-cardiology pipelines within national health-system infrastructures. First, although our cohort size (n = 136) compares favorably with previous translational studies, larger multicenter validation is needed to confirm generalizability across ethnic and clinical backgrounds. Second, only a preselected panel of seven miRNAs was analyzed; unbiased next-generation sequencing could uncover additional candidates involved in post-MI remodeling. Third, temporal sampling intervals may have missed transient fluctuations in miRNA release between subacute and chronic phases. Fourth, although CMR offers gold-standard remodeling quantification, logistical constraints limited complete 6-month follow-up imaging in all participants.

Advanced Journal of Biomedicine & Medicine
2025, Volume 13, Issue 2, Page 65-79
Available online: May 31, 2025
Journal homepage: www.ajbm.net

Finally, causality cannot be inferred; circulating miRNAs may be epiphenomena reflecting tissue injury rather than direct effectors. Nonetheless, their consistent correlation with structural outcomes strongly supports biological relevance.

The next stage of translational development should focus on prospective validation and mechanistic intervention. Ongoing European consortia are exploring miRNA-based risk algorithms and antisense-mediated inhibition (e.g., anti-miR-21 therapy) in patients with ischemic and non-ischemic cardiomyopathy [26]. Integration of machine-learning models combining miRNA panels, CMR parameters, and clinical data may further enhance prognostic precision [27,28]. Additionally, emerging extracellular-vesicle–derived miRNAs warrant investigation, as vesicle encapsulation may prolong stability and convey targeted intercellular signaling [29,30]. Ultimately, standardization of assay techniques, normalization controls, and reference ranges will be essential for clinical translation.

CONCLUSIONS

This study establishes that specific circulating miRNAs—particularly miR-21 and miR-29b—serve as robust biomarkers and potential mediators of adverse myocardial remodeling after infarction, while miR-133a signifies favorable repair. By integrating molecular and imaging data, we demonstrate that miRNA profiling provides early, non-invasive insight into the trajectory of ventricular recovery, enabling precision risk stratification. These findings support the incorporation of miRNA-based diagnostics into post-MI surveillance protocols and lay the foundation for future targeted antifibrotic therapies aimed at modifying the remodeling process and preventing heart failure.

AUTHOR CONTRIBUTIONS

Concept and Study Design

J.M. González-López and E. Martínez-Santos conceptualized the study, designed the research protocol, and supervised patient recruitment and data integration.

Data Collection and Experimental Work:

C.R. Fernández-Pérez and M.L. Ruiz-Delgado coordinated clinical sample processing, RNA extraction, and qRT-PCR assays.

A. Navarro-Torres contributed to the establishment of molecular and histological validation protocols.

Data Analysis and Interpretation:

E. Martínez-Santos and J.M. González-López performed statistical analysis and correlation modeling between circulating miRNAs and imaging indices.

M.L. Ruiz-Delgado contributed to imaging interpretation and translational integration of CMR findings.

Manuscript Preparation:

J.M. González-López drafted the manuscript. All co-authors reviewed and critically revised it for intellectual content.

All authors approved the final version and agree to be accountable for all aspects of the work.

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ETHICAL APPROVAL

This study was approved by the Comité de Ética de Investigación del Hospital Clínic de Barcelona (approval code: HCB-CardioMI-2022-0045) and conducted in accordance with the Declaration of Helsinki (2013 revision) and the Spanish Biomedical Research Act (Ley 14/2007 de Investigación Biomédica).

All participants provided written informed consent prior to inclusion. Data were anonymized following the principles of the European General Data Protection Regulation (GDPR, EU 2016/679).

CONFLICT OF INTEREST

The authors declare no financial or personal conflicts of interest that could have influenced the conduct or outcomes of this study.

Dr. González-López has received lecture honoraria from the Spanish Society of Cardiology (SEC) outside the submitted work.

All other authors report no competing interests.

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