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Original Article

Relationship between miR-148a-3p and Lower Extremity Arteriosclerosis Obliterans

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ABSTRACT

Background: Post-interventional restenosis remains a major limitation in the management of Lower Extremity Arteriosclerosis Obliterans (LEASO), and reliable circulating biomarkers for early risk prediction are still lacking. **Objectives:** This study aimed to investigate the relationship between serum miR-148a-3p expression and post-interventional restenosis in patients with LEASO, and to evaluate its potential as a predictive biomarker. **Materials and Methods:** A total of 412 LEASO patients who underwent endovascular intervention between May 2023 and November 2023 were enrolled. Serum miR-148a-3p expression was detected before intervention. All patients were followed up for 6 months to assess restenosis. Univariate and multivariate Cox proportional hazards regression analyses were used to identify independent risk factors for restenosis, and Receiver Operating Characteristic (ROC) curve analysis was performed. **Results:** During follow-up, 80 patients (19.4%) developed restenosis. The expression level of miR-148a-3p in the restenosis group was significantly higher (1.4±0.2 vs. 0.5±0.2, $p<0.001$). Older age (≥65 years), higher body mass index (BMI≥25 kg/m^2), hypertension, diabetes mellitus, coronary heart disease, and elevated miR-148a-3p (≥0.6) were identified as independent risk factors. ROC curve analysis showed that miR-148a-3p had good predictive performance for restenosis, with an Area Under the Curve (AUC) of 0.86, a sensitivity of 82.5%, and a specificity of 79.8% at the optimal cutoff value of 0.6. **Conclusion:** Serum miR-148a-3p is an independent predictor of post-interventional restenosis in LEASO patients. Its elevated expression may be involved in the pathogenesis of restenosis, suggesting its potential as a novel biomarker for risk stratification and clinical management of LEASO patients after intervention.

Keywords: Lower Extremity Arteriosclerosis Obliterans, Mechanism studies, miR-148a-3p, miRNA.

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INTRODUCTION

Lower Extremity Arteriosclerosis Obliterans (LEASO) is a prevalent and debilitating atherosclerotic disease characterized by the progressive stenosis or occlusion of the arteries supplying the lower limbs. This vascular insufficiency leads to a spectrum of clinical manifestations, ranging from intermittent claudication-pain induced by walking that resolves with rest-to more severe sequelae, which significantly impair quality of life and pose a high risk for limb loss.[1] With the global trends of population aging and the increasing prevalence of metabolic syndromes, the incidence and socioeconomic burden of LEASO continue to rise, establishing it as a major public health concern.

The management of symptomatic LEASO is multifaceted, encompassing lifestyle modifications, optimal medical therapy, and revascularization procedures. Endovascular interventions, including Percutaneous Transluminal Angioplasty (PTA) and stent implantation, have become first-line revascularization strategies due to their minimally invasive nature and lower periprocedural risk compared to open surgical bypass.[2,3] However, a significant clinical challenge following these interventions is restenosis, which occurs in a substantial proportion of patients within the first year and severely compromises long-term therapeutic efficacy.

However, the long-term success of these interventions is fundamentally limited by the frequent development of restenosis, a process of vascular re-narrowing at the treatment site. Restenosis represents a critical failure mode, occurring in a substantial proportion of patients, often within the first 6 to 12 months post-procedure, and severely compromises the durability of therapeutic efficacy, leading to symptom recurrence, repeat interventions, and increased healthcare costs. The pathogenesis of both native LEASO and post-interventional restenosis is

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multifactorial and intricately linked, involving a complex interplay of vascular biology responses. Key mechanisms include initial endothelial injury inflicted by the balloon or stent, which triggers a cascade of events: platelet adhesion and activation, recruitment of inflammatory cells, and the release of a milieu of cytokines, chemokines, and growth factors.[4,5] This inflammatory microenvironment drives medial Vascular Smooth Muscle Cells (VSMCs) from a quiescent state to a proliferative, and migratory phenotype. These activated VSMCs then migrate into the intima, undergo extensive proliferation, and produce abundant extracellular matrix, collectively leading to neointimal hyperplasia—the histological hallmark of restenosis. Traditional cardiovascular risk factors such as hypertension, hyperlipidemia, and chronic smoking are well-established contributors that exacerbate endothelial dysfunction, amplify the inflammatory response, and promote VSMC dysregulation, thereby accelerating both the atherosclerotic process and the subsequent restenotic pathway.[6] Despite advances in interventional techniques and pharmacotherapy, the molecular mechanisms underlying restenosis remain incompletely understood, limiting the development of targeted strategies to prevent its occurrence.

In recent years, microRNAs (miRNAs) have emerged as crucial post-transcriptional regulators of gene expression, offering new insights into disease mechanisms. MiRNAs are involved in virtually all biological processes, and their dysregulation has been implicated in various cardiovascular diseases.[7,8] They fine-tune key processes relevant to vascular pathology, such as inflammatory signaling, lipid metabolism, cellular apoptosis, and critically, the proliferation and migration of VSMCs and endothelial cells.[9,10]

Among the plethora of miRNAs, miR-148a-3p has attracted attention for its potential role in vascular biology. Preliminary evidence suggests its involvement in processes central to vascular remodeling and endothelial function.[11] For instance, studies have implicated miR-148a-3p in regulating cholesterol homeostasis and macrophage activation in atherosclerotic plaques. Furthermore, its expression has been reported to be altered in models of vascular injury and hypoxia. However, its specific expression pattern, functional role, and clinical relevance in the distinct context of LEASO, particularly concerning the critical endpoint of post-endovascular restenosis, are not well defined and represent a significant gap in knowledge. Therefore, this study aims to evaluate relationship between pre-procedural serum levels of miR-148a-3p and the occurrence of restenosis in patients undergoing endovascular treatment for LEASO. We further seek to evaluate its independent predictive value alongside conventional risk factors and to explore its potential utility. Elucidating the role of miR-148a-3p may not only enhance our understanding of restenosis pathogenesis but also pave the way for future therapeutic strategies aimed at modulating its activity to improve patient outcomes.

MATERIALS AND METHODS

Study Population and Patient Selection

A total of 412 consecutive patients diagnosed with LEASO who were admitted to our institution between May 2023 and November 2023 were enrolled in this study. The cohort consisted of 292 males and 120 females. All participants provided written informed consent. Inclusion Criteria: (1) Age≥18 years. (2) Diagnosis of lower extremity arterial stenosis or occlusion confirmed by Computed Tomography Angiography (CTA). (3) Baseline Ankle-Brachial Index (ABI) of less than 0.9. (4) Presence of typical clinical symptoms, such as intermittent claudication, rest pain, or tissue ischemia/gangrene. Exclusion Criteria: (1) History of prior interventional therapy (e.g., angioplasty, stenting, or bypass surgery) on the target limb. For patients with bilateral lesions, only the limb with the more severe stenosis was included for analysis. (2) Contraindications to antiplatelet or anticoagulant therapy. (3) Diagnosis of malignant tumors. (4) Severe renal insufficiency, defined as an estimated Glomerular Filtration Rate (eGFR)<30 mL/min/1.73 m^2 based on a stable value (confirmed by two measurements at least three months apart) or based on the first admission value if no prior medical records were available. (5) Presence of other severe systemic or chronic diseases (e.g., active infection, severe cardiac dysfunction) deemed to interfere with the study procedures or outcomes.

Methodologies

Interventional Treatment Protocol

All patients received standardized interventional therapy. Pre-treatment antiplatelet therapy (aspirin 100 mg/day and clopidogrel 75 mg/day) was initiated at least two days prior to the procedure. The choice of intervention was based on lesion characteristics: PTA was performed for lesions <3 cm, while stent implantation was employed for lesions ≥3 cm or if residual stenosis exceeded 30% after PTA. For total occlusions or lesions >10 cm, surgical alternatives were considered. Post-procedure, subcutaneous low-molecular-weight heparin was administered for three days, followed by long-term dual antiplatelet therapy.

Follow-up Assessment

All patients were followed up for 6 months post-intervention to assess the occurrence of restenosis. Follow-up evaluations included clinical assessment of symptoms, physical examination, and measurement of the Ankle-Brachial Index (ABI). Imaging follow-up was performed using duplex ultrasound or CTA at the 6-month visit, or earlier if clinically indicated due to symptom recurrence.

Restenosis was defined using the following criteria: (1) Imaging-based criteria: a Peak Systolic Velocity Ratio (PSVR)>2.4 on duplex ultrasound (correlating with a diameter stenosis ≥50%) or a diameter stenosis ≥50% confirmed by CTA;

or (2) Hemodynamic criteria: a decrease in the Ankle-Brachial Index (ABI) of ≥0.15 from the immediate post-procedure value, accompanied by recurrent clinical symptoms (e.g., intermittent claudication, rest pain). Patients meeting either criterion were classified as having developed restenosis.

Detection of Serum miR-148a-3p

Venous blood samples were collected from each patient 4 hr before the intervention. The detection of miR-148a-3p followed a two-step protocol.

Exosome Isolation

Serum was separated by centrifugation at 3,000 × g for 10 min. Exosomes were subsequently isolated from the supernatant using the ExoQuick™ Exosome Precipitation Kit (System Biosciences, Palo Alto, CA, USA) according to the manufacturer's instructions. To confirm the efficiency of exosome enrichment, the isolated particles were characterized by detecting exosomal surface markers (CD9, CD63, and CD81) using Western blotting.

RNA Extraction and qRT-PCR: Total RNA, including miRNA, was extracted from the isolated exosomes using TRIzol reagent (Invitrogen, Carlsbad, CA, USA). Complementary DNA (cDNA) was synthesized using a miR-148a-3p-specific reverse transcription primer (Tiangen Biotech). Quantitative real-time PCR (qRT-PCR) was performed on an ABI PRISM 7500 Sequence Detection System. The relative expression level of miR-148a-3p was calculated using the $2^{\wedge\text{-}\Delta\Delta Ct}$ method, with U6 snRNA as an internal control. The stability of U6 expression across different experimental groups was assessed prior to data analysis, and no significant variation was observed, confirming its suitability as a normalizer in this study.

Statistical Analysis

Statistical analyses were performed using Statistic Package for Social Science (SPSS) software (version 22.0, Chicago, IL, USA). Continuous variables are presented as mean±standard deviation. Categorical variables are presented as numbers (percentages). The predictive value of miR-148a-3p for restenosis was assessed using Receiver Operating Characteristic (ROC) curve analysis. To identify independent risk factors for restenosis, both univariate and multivariate Cox proportional hazards regression analyses were performed. Variables with a p value <0.1 in the univariate analysis were entered into the multivariate Cox model. Results are presented as Hazard Ratios (HR) with 95% Confidence Intervals (CI). A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

A total of 412 patients with Lower Extremity Arteriosclerosis Obliterans (LEASO) were enrolled in this study. The mean age of the patients was 61.2±5.8 years. The cohort presented with a mean Low-Density Lipoprotein Cholesterol (LDL-C) level of 2.68±0.18 mmol/L. Comorbidities were prevalent, including hypertension (44.7%), diabetes mellitus (29.6%), and coronary heart disease (31.6%). The mean expression level of serum miR-148a-3p for the entire cohort was 0.78±0.42. The baseline clinical and demographic characteristics of the cohort are summarized in Table 1.

The Predictive Value of Serum miR-148a-3p for Restenosis

During the 6-month follow-up period, 80 patients (19.4%) developed restenosis. The expression level of serum miR-148a-3p was significantly higher in patients who developed restenosis (1.4±0.2 vs. 0.5±0.2, p<0.001). ROC curve analysis indicated that miR-148a-3p had a significant predictive value for restenosis, with an Area Under the Curve (AUC) of 0.86 (95% CI: 0.82-0.90). At an optimal cutoff value of 0.6, with a sensitivity of 82.5% and the specificity of 79.8% (Figure 1).

Development and Validation of a Predictive Model for Restenosis

To construct and validate a predictive model, the entire cohort was randomly divided into a training set (n=288, 70%) and a validation set (n=124, 30%). There was no significant difference in baseline characteristics between the two sets (p>0.05) (Table 2).

In the training set, univariate Cox regression analysis identified several factors associated with restenosis, including age, BMI, hypertension, diabetes, coronary heart disease, and miR-148a-3p expression (≥0.6). These variables were subsequently entered into a multivariate Cox proportional hazards model. The results confirmed that age ≥65 years, BMI≥25 kg/m², hypertension, diabetes, and elevated miR-148a-3p (≥0.6) were independent risk factors for restenosis (p<0.05).

DISCUSSION

The present study provides compelling evidence that elevated serum levels of miR-148a-3p are significantly and independently associated with an increased risk of restenosis within 6 months following endovascular intervention in patients with LEASO. By integrating this molecular biomarker with established clinical risk factors, we developed a predictive model that demonstrated robust discriminatory ability. These findings contribute to the evolving narrative of personalized medicine in vascular disorders, suggesting that circulating miRNAs, particularly miR-148a-3p, may serve as valuable tools for risk stratification and prognostication in a clinical setting fraught with the challenge of post-interventional failure.

Our data indicate that patients in the restenosis group had a significantly higher burden of traditional cardiovascular risk

factors. This aligns with extensive previous research identifying advanced age, metabolic disorders, and hypertension as significant contributors to atherosclerosis progression and abnormal vascular repair after intervention.[12,13] For instance, a hyperglycemic state can exacerbate endothelial injury and inflammation through pathways involving advanced glycation end products, while the sustained hemodynamic shear stress from hypertension directly promotes phenotypic switching and proliferation of vascular smooth muscle cells.[14] The observed association between higher miR-148a-3p expression and restenosis aligns with the burgeoning understanding of miRNAs as master regulators of vascular pathophysiology. Restenosis is fundamentally a maladaptive response to vessel injury, characterized by a cascade of events: endothelial denudation, platelet activation and inflammatory cell recruitment, release of growth factors, and subsequent phenotypic modulation, proliferation, and migration of vascular smooth muscle cells from the media into the intima, culminating in neointimal hyperplasia. Our results reaffirm the fundamental importance of comprehensive management of these traditional risk factors for improving the prognosis of ASO patients, particularly those undergoing interventional therapy.

We found that pre-procedural serum miR-148a-3p levels were significantly elevated in patients who subsequently developed restenosis, with an AUC of 0.86, demonstrating good discriminatory power. MicroRNAs, as key post-transcriptional regulators of gene expression, play multifaceted roles in vascular biology. Prior studies suggest that miR-148 is involved in regulating cell proliferation, apoptosis, and inflammatory responses.[15,16] For example, one research reported upregulated

Table 1: The baseline characteristics of the restenosis group versus the non-restenosis group.

Variable	Restenosis group (*n*=80)	Non-restenosis group (*n*=332)	T/X²	*p*
Age	65.06±2.03	59.99±2.25	18.425	<0.001
Male (example, %)	56(70.00)	240(72.29)	0.167	0.683
BMI (kg/m²)	22.9±1.9	29.1±2.5	20.775	<0.001
Course of disease (years)	3.4±1.9	3.8±2.2	1.497	0.135
Smoking (example, %)	58(72.50)	210(63.25)	2.425	0.119
Diabetes mellitus (case, %)	46(57.50)	76(22.89)	37.045	<0.001
Hypertension (case, %)	46(57.50)	138(41.57)	6.622	0.010
LDL-C (mmol/L)	2.6±0.2	2.7±0.1	6.392	<0.001
Coronary heart disease (case, %)	40(50.00)	90(27.11)	15.642	<0.001
Treatment			1.004	0.605
PTA	41(51.3)	167(50.30)		
Stent implantation	29(36.2)	109(32.83)		
operation	10(12.5)	56(16.87)		
miR-148a-3p expression	1.4±0.2	0.5±0.2	36.131	<0.001

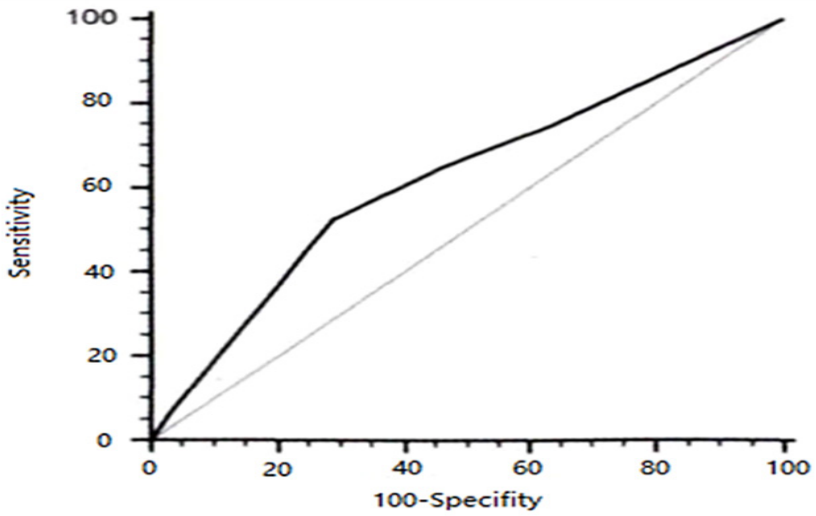

Figure 1: ROC curves of serum miR-148a-3p for predicting restenosis in LEASO patients.

Table 2: Multivariate Cox Regression Analysis for Restenosis in the Training Set.

Variable	HR (95% CI)	*p*
Age (≥65 vs<65, years)	1.05(1.04-1.07)	<0.001
BMI (≥25 vs<25, kg/m^2)	1.04(1.02-1.06)	<0.001
Hypertension (Yes vs. No)	1.09(1.07-1.12)	<0.001
Diabetes (Yes vs. No)	1.12(1.08-1.16)	<0.001
Coronary heart disease (Yes vs. No)	1.05(1.02-1.08)	<0.001
miR-148a-3p (≥0.6 vs<0.6)	2.91(1.34-6.06)	<0.001

expression of miR-148a-3p in the neointima following vascular injury, potentially promoting the migration of vascular smooth muscle cells by targeting key molecules in pathways such as PI3K/Akt or TGF-β signaling.[17] Our research directly links miR-148a-3p to the specific clinical scenario of post-interventional restenosis in LEASO, adding to the evidence for this miRNA in the field of peripheral artery disease and suggesting its potential as a novel circulating biomarker for monitoring vascular injury and repair status.

Through multivariate Cox regression analysis, we integrated miR-148a-3p with key clinical variables such as age, BMI, hypertension, and diabetes to build a risk prediction model for restenosis. This integrated approach holds greater clinical utility than relying on any single indicator, including miR-148a-3p alone. Our model indicates that combining the molecular biomarker miR-148a-3p with traditional risk factors enables more precise risk stratification. This provides a preliminary basis for future implementation of individualized post-procedural monitoring and management strategies, such as intensified follow-up for high-risk patients or exploration of enhanced anti-proliferative therapies.[18] However, as some risk factors in the model are already part of routine clinical assessment, the incremental value of the model needs further validation of its cost-effectiveness in prospective, large-scale studies.

Delving into the potential mechanistic underpinnings, miR-148a-3p is a member of a miRNA family implicated in cell cycle regulation, apoptosis, and differentiation across various tissues. In the vascular context, its proposed roles become highly relevant. First, a primary suspect mechanism is the direct regulation of VSMC behavior. Bioinformatics analyses and prior studies in other vascular models suggest that miR-148a-3p can target several genes involved in maintaining VSMC contractility and suppressing proliferation. Second, beyond VSMCs, the integrity and reparative capacity of the endothelium are paramount. A timely and effective re-endothelialization is the body's natural barrier against unrestrained neointimal growth. miRNAs are critical for endothelial function, influencing angiogenesis, permeability, and inflammatory adhesion. Elevated miR-148a-3p may impede endothelial repair by targeting genes involved in endothelial cell migration or capillary tube formation. Moreover, endothelial dysfunction is a key initiator of atherosclerosis and restenosis. miR-148a-3p might modulate the expression of adhesion molecules like VCAM-1 or ICAM-1 on endothelial cells, thereby influencing the initial recruitment of monocytes and lymphocytes to the site of injury. This would place miR-148a-3p at a very early stage in the restenosis cascade, amplifying the inflammatory insult that sets the stage for later hyperplasia. Third, the inflammatory axis cannot be overlooked. The early inflammatory response to vessel injury sets the stage for subsequent repair or maladaptive remodeling. Evidence suggests miR-148a-3p can influence macrophage polarization, potentially skewing it towards a sustained M1 state, perpetuating a pro-inflammatory microenvironment rich in cytokines like IL-1β, TNF-α, and MCP-1. Additionally, miR-148a-3p could modulate T-cell differentiation. The systemic elevation of miR-148a-3p, as measured in serum, likely reflects not just vascular cell secretion but also release from circulating or resident immune cells, making it an integrative biomarker of a pro-restenotic systemic state.

However, this study has several limitations. First, it is a single-center, observational study, which may introduce selection bias. Second, the sample size is relatively limited, particularly the number of restenosis events, which may affect the stability of the model estimates, especially for some covariates. Third, the follow-up period was only 6 months, failing to assess longer-term restenosis outcomes. Fourth, the mechanistic investigation remains at the associative level, lacking functional experiments to confirm the direct role of miR-148a-3p. Future research should first prospectively validate the generalizability of this predictive model in multicenter, large-scale cohorts. Second, extending the follow-up duration is necessary to clarify the predictive value of miR-148a-3p for long-term prognosis. Third, there is a pressing need to elucidate the specific target genes and signaling pathways through which miR-148a-3p regulates restenosis. Finally, exploring whether targeting miR-148a-3p can delay or prevent restenosis in animal models would lay the groundwork for developing novel therapeutic strategies.

CONCLUSION

In summary, this study confirms that serum miR-148a-3p is an independent risk factor for restenosis following endovascular intervention in LEASO patients. Furthermore, the combined clinical-molecular prediction model based on this biomarker demonstrates good risk discrimination ability. These findings add a new perspective to understanding the pathogenesis of restenosis. Looking further ahead, if miR-148a-3p is confirmed as a key driver, it opens therapeutic avenues. miRNA-based therapeutics, though still emerging, hold promise. Local delivery of a miR-148a-3p inhibitor via drug-eluting balloon or stent coating could provide targeted, site-specific therapy to modulate the healing response towards favorable remodeling, complementing current anti-proliferative drugs. This approach

could potentially offer a better safety profile by avoiding systemic effects. Furthermore, understanding the upstream regulators of miR-148a-3p could reveal novel, more conventional pharmacological targets to indirectly modulate its expression.

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Not applicable.

ABBREVIATIONS

LEASO: Lower extremity arteriosclerosis obliterans; **ROC:** Receiver operating characteristic; **AUC:** Area under the curve; **BMI:** Body mass index; **miRNA:** MicroRNA; **PTA:** Percutaneous transluminal angioplasty; **CTA:** Computed tomography angiography; **ABI:** Ankle-brachial index; **PSVR:** Peak systolic velocity ratio; **VSMCs:** Vascular smooth muscle cells; **ECM:** Extracellular matrix; **LDL-C:** Low-density lipoprotein cholesterol; **qRT-PCR:** Quantitative real-time polymerase chain reaction; **cDNA:** Complementary DNA; **RNA:** Ribonucleic acid; **U6:** U6 small nuclear RNA; **SPSS:** Statistical Package for the Social Sciences; **HR:** Hazard ratio; **CI:** Confidence interval; **TNF-α:** Tumor necrosis factor alpha; **IL:** Interleukin; **MCP-1:** Monocyte chemoattractant protein-1; **VCAM-1:** Vascular cell adhesion molecule-1; **ICAM-1:** Intercellular adhesion molecule-1; **PI3K:** Phosphoinositide 3-kinase; **Akt:** Protein kinase B; **TGF-β:** Transforming growth factor beta; **M1:** Classically activated macrophage phenotype.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

Not applicable.

ETHICAL STATEMENT

This study was approved by the ethics committee of the Second Affiliated Hospital of Soochow University. Signed written informed consents were obtained from the patients and/or guardians. This study was conducted in accordance with the Declaration of Helsinki.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

SUMMARY

This study investigated the association between serum miR-148a-3p expression and post-interventional restenosis in patients with Lower Extremity Arteriosclerosis Obliterans (LEASO), and evaluated its predictive value as a circulating biomarker. A total of 412 patients undergoing endovascular intervention were enrolled and followed for 6 months. Serum miR-148a-3p levels were measured prior to the procedure, and restenosis was assessed using imaging and hemodynamic criteria. The results showed that patients who developed restenosis exhibited significantly higher miR-148a-3p expression compared to those without restenosis. Multivariate Cox regression analysis identified elevated miR-148a-3p, along with age, body mass index, hypertension, and diabetes, as independent risk factors. Receiver operating characteristic analysis demonstrated good predictive performance, with an AUC of 0.86. These findings suggest that miR-148a-3p may play a role in the pathogenesis of restenosis and could serve as a novel biomarker for risk stratification and individualized management in LEASO patients after intervention.

REFERENCES

1. Clark GP. Treatment options for symptomatic knee osteoarthritis in adults. Jaapa-J Am Acad Phys. 2023;36(11):1-6. Available from: https://pubmed.ncbi.nlm.nih.gov/37884044/
2. Hinman RS, Hall M, Comensoli S, Bennell KL. Exercise and Sports Science Australia (ESSA) updated Position Statement on exercise and physical activity for people with hip/knee osteoarthritis. J Sci Med Sport. 2023;26(1):37-45. Available from: https://pubmed.ncbi.nlm.nih.gov/36463000/
3. Uritani D, Koda H, Yasuura Y, Kusumoto A. Factors associated with subjective knee joint stiffness in people with knee osteoarthritis: A systematic review. Int J Rheum Dis. 2023;26(3):425-36. Available from: https://pubmed.ncbi.nlm.nih.gov/36572505/
4. Lin X, Chen J, Qiu P, Zhang Q, Wang S, Su M, *et al.* Biphasic hierarchical extracellular matrix scaffold for osteochondral defect regeneration. Osteoarthr Cartilage. 2018;26(3):433-44. Available from: https://pubmed.ncbi.nlm.nih.gov/29233641/
5. Ma P, Yue L, Yang H, Fan Y, Bai J, Li S, *et al.* Chondroprotective and anti-inflammatory effects of amurensin H by regulating TLR4/Syk/NF-κB signals. J Cell Mol Med. 2020;24(2):1958-68. Available from: https://pubmed.ncbi.nlm.nih.gov/31876072/
6. Alhasan MK, Obeidat N, Al Bdour IR, Al Zeghari MJ, Al-Othman LE. Radiographic predictors of knee osteoarthritis. Radiography (London, England: 1995). 2025;31(5):103086. Available from: https://pubmed.ncbi.nlm.nih.gov/40639313/
7. Cheng H, Hao B, Sun J, Yin M. C-Terminal Cross-Linked Telopeptides of Type II Collagen as Biomarker for Radiological Knee Osteoarthritis: A Meta-Analysis. Cartilage. 2020;11(4):512-20. Available from: https://pubmed.ncbi.nlm.nih.gov/30221987/
8. Lei J, Deng H, Ran Y, Lv Y, Amhare AF, Wang L, *et al.* Altered Expression of Aggrecan, FAM20B, B3GALT6, and EXTL2 in Patients with Osteoarthritis and Kashin-Beck Disease. Cartilage. 2021; 13(1_suppl):818S-28S. Available from: https://pubmed.ncbi.nlm.nih.gov/32517548/
9. Zhu B, Cui G, Zhang Q, Cheng X, Tang S. Desumoylation of aggrecan and collagen II facilitates degradation via aggrecanases in IL-1β-mediated osteoarthritis. J Pain Res. 2019;12:2145-53. Available from: https://pubmed.ncbi.nlm.nih.gov/31372032/
10. Filippiadis D, Soulez G, Cornelis FH. Genicular artery embolization for symptomatic knee osteoarthritis: New perspectives on the temporary-permanent dilemma. Diagn Interv Imag. 2024;105(4):125-6. Available from: https://pubmed.ncbi.nlm.nih.gov/38142181/
11. Hu Q, Ecker M. Overview of MMP-13 as a Promising Target for the Treatment of Osteoarthritis. International Journal of Molecular Sciences. 2021;22(4):1742. Available from: https://pubmed.ncbi.nlm.nih.gov/33572320/
12. Aneja A, Adams SB, Foster JA, Pezold R. AAOS Technology Overview Summary: Concentrated Bone Marrow Aspirate for Knee Osteoarthritis. The Journal of the American Academy of Orthopaedic Surgeons. 2023;31(1):e9-13. Available from: https://pubmed.ncbi.nlm.nih.gov/36473210/
13. Kenny RT, Murray B. Obesity-related knee osteoarthritis: a role for the rheumatology advanced nurse practitioner in Ireland. British Journal of Nursing (Mark Allen Publishing). 2024;33(9):418-23. Available from: https://pubmed.ncbi.nlm.nih.gov/38722014/
14. Zhu H, Yan X, Zhang M, Ji F, Wang S. miR-21-5p protects IL-1β-induced human chondrocytes from degradation. J Orthop Surg Res. 2019;14(1):118. Available from: https://pubmed.ncbi.nlm.nih.gov/31053150/
15. Wang B, Jiang Y, Yao Z, Chen P, Yu B, Wang S. Aucubin Protects Chondrocytes Against IL-1β-Induced Apoptosis *in vitro* and Inhibits Osteoarthritis in a Mouse Model. Drug Des Dev Ther. 2019;13:3529-38. Available from: https://pubmed.ncbi.nlm.nih.gov/31631977/

16. Zhao Y, Li Y, Qu R, Chen X, Wang W, Qiu C, *et al.* Cortistatin binds to TNF-α receptors and protects against osteoarthritis. Ebiomedicine. 2019;41:556-70. Available from: https://pubmed.ncbi.nlm.nih.gov/30826358/
17. Shang X, Böker KO, Taheri S, Hawellek T, Lehmann W, Schilling AF. The Interaction between microRNAs and the Wnt/β-Catenin Signaling Pathway in Osteoarthritis. International Journal of Molecular Sciences. 2021;22(18):9887. Available from: https://pubmed.ncbi.nlm.nih.gov/34576049/
18. Yu H, Liu Y, Yang X, He J, Zhang F, Zhong Q, *et al.* Strontium ranelate promotes chondrogenesis through inhibition of the Wnt/β-catenin pathway. Stem Cell Res Ther. 2021;12(1):296. Available from: https://pubmed.ncbi.nlm.nih.gov/34016181/

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