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# CHANGES IN INFLAMMATORY FACTORS (IL-6, IL-10, IL-1β, AND TNF-α) AND THEIR CORRELATION WITH MIRNAS EXPRESSION IN PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

## PROMENE INFLAMATORNIH FAKTORA (IL-6, IL-10, IL-1β I TNF-α) I NJIHOVA POVEZANOST SA EKSPRESIJOM MIRNK KOD PACIJENATA KOJI SU PODVRGNUTI PERKUTANOJ KORONARNOJ INTERVENCIJI

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## Summary

**Background:** Percutaneous coronary intervention (PCI) can induce vascular injury and inflammatory responses. miRNAs are involved in vascular homeostasis and repair processes, but their interactions with inflammatory factors following PCI remain poorly defined. The objective of this study was to determine the changes in inflammatory factors in PCI patients and their correlation with the expression of specific miRNAs.

**Methods:** Patients undergoing PCI were selected as the observation group (AG), and healthy individuals undergoing physical examinations as the control group (BG). Serum inflammatory factors were quantified by ELISA. RT-qPCR was utilized to assess the associations between inflammatory factors and miRNAs expression.

**Results:** IL-6, IL-10, IL-1β, and TNF-α were markedly elevated in the AG versus the BG; in the AG, the expression of miRNA-21 was significantly up-regulated, while the expression of miRNA-92a and miRNA-126 was significantly down-regulated ($P<0.05$). Correlation analysis showed that IL-6, IL-10, IL-1β, and TNF-α levels were positively correlated with miRNA-21 expression and negatively correlated with miRNA-92a and miRNA-126 expression.

**Conclusion:** Inflammatory responses are significantly activated in patients after PCI, accompanied by changes in miRNA expression profiles. Pro-inflammatory factors are positively associated with miRNA-21 and negatively

## Kratak sadržaj

**Uvod:** Perkutana koronarna intervencija (PCI) može izazvati oštećenje krvnih sudova i inflamatorni odgovor. MikroRNK (miRNK) učestvuju u održavanju vaskularne homeostaze i procesima reparacije, ali njihova povezanost sa inflamatornim faktorima nakon PCI još uvek nije dovoljno razjašnjena. Cilj ovog istraživanja je bio da se ispitaju promene inflamatornih faktora kod pacijenata podvrgnutih PCI i njihova povezanost sa ekspresijom specifičnih miRNK.

**Metode:** Pacijenti koji su podvrgnuti PCI činili su grupu ispitanika (AG), dok su zdrave osobe koje su bile na sistematskim pregledima činile kontrolnu grupu (BG). Serumske koncentracije inflamatornih faktora određivane su ELISA metodom. Metoda reverzne transkripcije i kvantitativne lančane reakcije polimeraze (RT-qPCR) je korišćena za ispitivanje povezanosti između inflamatornih faktora i ekspresije miRNK.

**Rezultati:** Nivoi IL-6, IL-10, IL-1β i TNF-α su bili značajno povišeni u AG u poređenju sa BG. U AG je ekspresija miRNK-21 bila značajno povećana, dok je ekspresija miRNK-92a i miRNK-126 bila značajno smanjena ($P<0,05$). Korelaciona analiza pokazala je da su nivoi IL-6, IL-10, IL-1β i TNF-α pozitivno korelisali sa ekspresijom miRNK-21, a negativno sa ekspresijom miRNK-92a i miRNK-126.

**Zaključak:** Inflamatorni odgovor je značajno aktiviran kod pacijenata nakon PCI i praćen je promenama u profilima

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associated with miRNA-92a and miRNA-126, reflecting their joint involvement in the damage and repair of blood vessels after surgery.

**Keywords:** percutaneous coronary intervention, inflammatory factors, miRNAs expression, correlation

ekspresije miRNK. Proinflamatorni faktori su pozitivno povezani sa miRNK-21, a negativno sa miRNK-92a i miRNK-126, što ukazuje na njihovu zajedničku ulogu u oštećenju i reparaciji krvnih sudova nakon intervencije.

**Ključne reči:** perkutana koronarna intervencija, inflamatorni faktori, ekspresija miRNK, korelacija

## Introduction

Percutaneous coronary intervention (PCI) is an important method for treating coronary artery disease (CAD). This surgery restores myocardial blood flow perfusion and improves clinical symptoms by balloon dilation and stent implantation, especially in the treatment of acute coronary syndrome (ACS) (1, 2). However, during PCI, balloon dilation and stent placement can easily cause plaque rupture and thrombosis, which can mechanically damage the vascular endothelium and trigger an inflammatory response (3–5).

Pro-inflammatory factors obviously increase during the perioperative period of PCI, while anti-inflammatory factors may be relatively insufficient. This can lead to further endothelial dysfunction, increased plaque instability, atherosclerosis, and restenosis, all of which are harmful to the patient's health. miRNAs have become a hot topic in cardiovascular disease research. miRNAs modulate vascular endothelial function and affect the proliferation and migration of smooth muscle cells, thereby influencing the inflammatory response. The expression levels of several miRNAs have been shown to correlate with CAD severity, plaque stability, and patient prognosis. Some miRNAs can change their expression in response to inflammatory stimuli. Tong et al. treated human aortic endothelial cells (HAEC) from ACS patients with 20 μg/mL 7-ketocholesterol (7-KC) and observed a pronounced elevation in miR-134-5p (6). In 7-KC-treated HAEC, knockdown of miR-134-5p weakened the inhibition of endothelial nitric oxide synthase and the activation of AKT, while mitigating the reduction of VE-cadherin and the induction of E-selectin. Tang et al. (7) explored the mechanism by which miR-148a-3p alleviates CAD by inhibiting vascular endothelial cell (VEC) injury. The results showed that in lipopolysaccharide-induced VEC experiments, miR-148a-3p inhibited the upregulation of PCSK-9, thereby inhibiting NF-κB signaling and promoting VEC proliferation. Overexpression of PCSK-9 and the addition of NF-κB signaling pathway activators increased VEC apoptosis, demonstrating that miR-148a-3p protects VEC and alleviates CAD by down-regulating PCSK-9 to inhibit NF-κB signaling. More than 50 miRNAs have been identified as critical modulators of vascular homeostasis and CAD development, thereby contributing to atherosclerotic plaque formation, endothelial cell senescence, and disruption of vascular repair mechanisms (8).

The purpose of this study is to elucidate changes in key inflammatory factors and miRNA expression in people after PCI, analyze their correlations, and provide new experimental evidence to elucidate the molecular mechanisms of inflammatory responses after PCI.

## Material and Methods

The research subjects were sourced from the Department of Cardiology and the Physical Examination Department of Fengjie County People's Hospital from November 2024 to June 2025, including 34 patients who underwent PCI in the Department of Cardiology and 31 normal subjects who underwent physical examinations in the Physical Examination Department. The control group (BG) comprised normal subjects from the Physical Examination Department, while the observation group (AG) comprised PCI patients from the Department of Cardiology. The average age of the BG was 60.18 ± 6.22 years, with 23 males and 11 females; the average age of the AG was 59.26 ± 6.16 years, with 20 males and 11 females. No statistically significant differences were observed in the general information of the participants ($P>0.05$), and they were comparable. All research subjects voluntarily signed informed consent forms. All experimental operations were approved by the Medical Ethics Committee of Fengjie County People's Hospital.

Inclusion criteria: (1) Complete medical records; (2) Age > 18 years; (3) Signed informed consent form.

Exclusion criteria: (1) Presence of other cardiovascular diseases; (2) Presence of immune diseases; (3) Presence of other major organ diseases; (4) Presence of mental illness; (5) Currently participating in other drug studies

Materials: Protease K (Shanghai Tianwu Technology Co., Ltd., China); Trizol (Beijing Baiao Laibo Technology Co., Ltd., China); Chloroform, isopropanol, anhydrous ethanol (Wuhan Servicebio Technology Co., Ltd., China); Diethyl pyrocarbonate (DEPC) (Hubei Jiahui Xingcheng Biotechnology

Co., Ltd., China); miRNA reverse transcription and amplification kit (Gene Copoeia, USA).

Instruments: Fully automatic multifunctional enzyme-linked immunosorbent analyzer (Hangzhou YoMim Instrument Co., Ltd., China); Centrifuge (Changsha Yingtai Instrument Co., Ltd., China); Constant-temperature incubator (Beijing Taihongjun Instrument Co., Ltd., China); Polymerase chain reaction instrument (Shanghai Qiqian Electronic Technology Co., Ltd., China); Spectrophotometer (Shanghai Yuanxi Instrument Co., Ltd., China).

The AG underwent PCI, with the surgical procedure as follows: the patient's right radial artery was selected as the access route. The puncture area was strictly disinfected and covered with a sterile surgical drape. After determining the puncture point based on anatomical positioning, a small incision was made in the skin with a sterile scalpel. A puncture needle was precisely inserted into the radial artery. Upon observing bright red arterial blood flowing back to the needle hub, a soft and flexible guidewire was smoothly inserted along the needle lumen. A vascular sheath assembly with an inner and outer sheath was then slowly advanced along the guidewire and ultimately placed into the radial artery. The inner sheath and guidewire were subsequently removed, leaving the outer sheath as a stable channel for subsequent instruments. Through this outer sheath, a guidewire and angiographic catheter combination dedicated to coronary angiography was slowly inserted into the vascular lumen. Under guidewire guidance, the catheter was retrogradely advanced along the radial, brachial, and subclavian arteries into the root of the ascending aorta. The catheter position was confirmed in real time using X-ray fluoroscopy to avoid entering branches or causing vasospasm. When the angiographic catheter was successfully inserted into the left or right coronary artery ostium, it was connected to a three-way stopcock containing a pressure monitoring device, a continuous infusion of heparinized saline to prevent thrombosis, and a reserve of contrast agent. The pressure waveform in the aortic root was closely monitored, and an appropriate amount of contrast agent was injected through the three-way stopcock. Digital subtraction angiography (DSA) was used to visualize the coronary arteries in real time, enabling clear assessment of the anatomical structure, lesion location, degree of stenosis, and extent of involvement of each vessel.

For lesions with significant stenosis affecting myocardial perfusion, a treatment guidewire was replaced, and a balloon dilation catheter of appropriate size was advanced along it to the stenosis. A high-pressure injection pump was connected, and the balloon was gradually inflated to flatten the plaque and expand the lumen. Subsequently, a metal stent pre-mounted on the delivery system was precisely delivered to the lesion site. The balloon was again inflated using a pressure pump to fully deploy and release the stent, providing permanent vascular support. Successful stent placement, adequate expansion, and restoration of target lesion blood flow to TIMI-3 grade were confirmed by repeat angiography. At the end of the surgery, the angiographic catheter, guidewire, and vascular sheath were sequentially removed. The puncture site was covered with sterile gauze, and moderate manual pressure was applied to stop bleeding. A dedicated radial artery compressor was then used for timed and controlled compression dressing to prevent local bleeding or hematoma formation. Postoperatively, patients were closely monitored and received standard secondary prevention treatments, including dual antiplatelet therapy and statins.

Inflammatory factors and miRNAs expression were measured in both the BG and the AG 72 h after surgery to analyze their correlation.

*Inflammatory factor determination*

5 mL of fasting cubital vein blood was collected from both the BG and the AG after surgery. Centrifugation of the blood was carried out (3,500 r/min, 10 min). The levels of IL-6, IL-10, TNF-$\alpha$, and IL-1$\beta$ were measured using ELISA.

*miRNAs expression determination*

250 $\mu$L of plasma was taken and digested with proteinase K. Total RNA was extracted using the Trizol-chloroform method, precipitated with isopropanol, washed with 70% ethanol, and finally dissolved in DEPC water. The concentration and purity of RNA were measured using NanoDrop. Subsequently, reverse transcription was carried out: The RNA was first subjected to poly (A) tail addition (37 °C, 30 min), and then reverse-transcribed into cDNA at 42 °C using Oligo (dT) as the primer. The cDNA was diluted and used for RT-qPCR. The reaction system contained SYBR Green Mix, specific primers, and cDNA. The amplification conditions were: pre-denaturation (95 °C, 5 min), followed by 40 cycles (95 °C, 15 s; 56 °C, 45 s). Following amplification, the reaction specificity was assessed, with U6 snRNA serving as the reference for normalization to calculate the relative expression levels of the target miRNAs.

*Statistical processing*

Data were statistically analyzed utilizing SPSS 22.0. Measurement data were represented as mean $\pm$ SD. An independent samples t-test was adopted for data meeting the normal distribution

and homogeneity of variance, while non-parametric tests were adopted for data not meeting the criteria. The count data were analyzed using $\chi^2$ test. A significance threshold of $P<0.05$ was applied for all statistical assessments.

## Results

*Assessment of cytokines*

IL-6, IL-10, IL-1β, and TNF-α were evidently elevated in the AG versus the BG ($P<0.05$) (*Figure 1*). IL-1β and TNF-α are mainly released by activated monocytes/macrophages and endothelial cells. They initiate the inflammatory cascade after vascular injury, promoting the adhesion and infiltration of white blood cells and the development of inflammation. IL-6 is a multifunctional cytokine involved in the production of acute-phase proteins. Its elevation reflects the degree of endothelial injury caused by surgical trauma and the plaque burden. IL-10 was also evidently increased in PCI patients. This may be a compensatory anti-inflammatory mechanism initiated by the body to balance excessive inflammatory responses. However, its level cannot fully offset the pro-inflammatory state, and an overall pro-inflammatory predominance persists. The simultaneous increase of the four cytokines indicated an inflammatory response after PCI. PCI is mainly used to treat coronary atherosclerotic heart disease. The core pathological basis is atherosclerosis in the coronary arteries, leading to stenosis or occlusion of the vascular lumen and causing myocardial ischemia, hypoxia, or necrosis. These diseases include angina and myocardial infarction (MI).

PCI can trigger a systemic inflammatory response (9). Elevated con-centrations of IL-6, hs-CRP, and TNF-α in peripheral blood may serve as significant predictors for major adverse cardiovascular events and short-term clinical outcomes after PCI in patients with early-onset acute MI (AMI). Stent implantation induces cytokine production. The combined secretion of IL-1α, IL-8, and TNF-α, or the selective release of IL-8 and TNF-α alone, can better predict the outcome of stent implantation in AMI patients with non-ST-segment elevation MI and CAD, respectively (10). Cytokine-inhibiting drugs should be selected with caution to inhibit further cardiovascular damage.

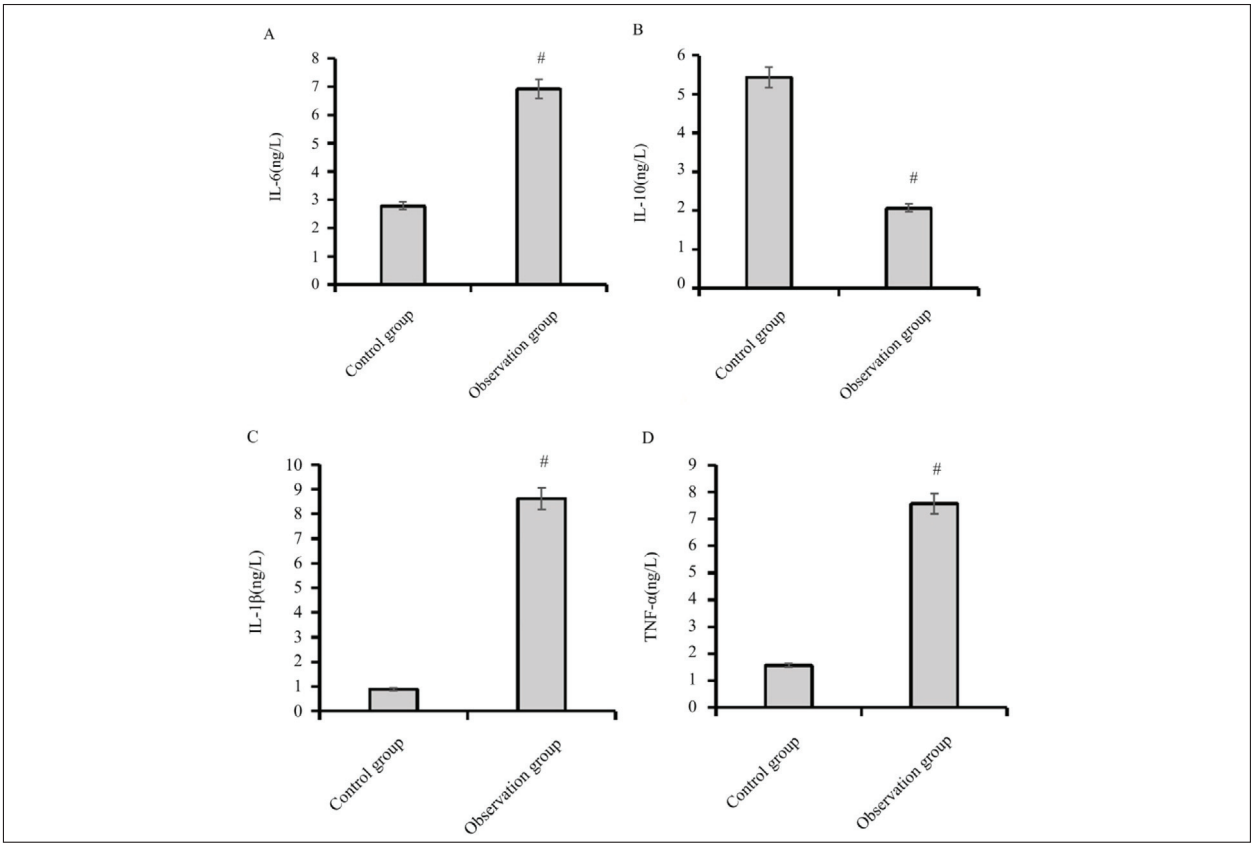


**Figure 1** Analysis of inflammatory factors.
Note: (A) IL-6; (B) IL-10; (C) IL-1β; (D) TNF-α. #relative to the BG, $P < 0.05$

In contrast to patients with angina, those with AMI exhibit a pronounced pro-inflammatory shift, characterized by elevated levels of key cytokines and adhesion molecules, alongside reduced levels of anti-inflammatory mediators (11). Elevated levels of key pro-inflammatory cytokines are an independent risk factor for major adverse cardiovascular events in AMI patients. They may provide new auxiliary indicators for predicting the prognosis of AMI patients.

*miRNAs expression*

miRNA-21 was evidently elevated in the AG versus the BG; miRNA-92a and miRNA-126 were evidently lower in the AG versus the BG ($P<0.05$) (*Figure 2*). These results revealed the molecular mechanisms underlying vascular biological responses after PCI. The upregulation of miRNA-21 was closely associated with the proliferation, migration, and anti-apoptotic effects of vascular smooth muscle cells. The up-regulation of miRNA-21 after PCI reflected the reparative response of the vascular wall to mechanical injury. By inhibiting target genes such as PTEN and PDCD4, it can promote cell survival. However, long-term overexpression might lead to neointimal multiplication and in-stent restenosis. miRNA-92a is mainly expressed by endothelial and immune cells. The significant decrease observed in PCI patients in this study might be related to early postoperative endothelial dysfunction, leading to reduced release or negative feedback regulation, or to patient drug intervention. miRNA-126 is a protective factor for promoting vascular repair. The decreased expression indicated that balloon dilation and stent placement during PCI caused endothelial injury. Its ability to regulate the VEGF and PI3K/Akt pathways was reduced, affecting endothelial regeneration and anti-inflammatory functions. Occupational noise exposure duration is evidently negatively correlated with heart rate variability indices, while occupational noise exposure duration is evidently associated with lower expression of miR-92a-3p and miR-21-5p (12). Occupational noise exposure is negatively correlated with miRNA-92a-3p, and noise exposure is positively correlated with systolic and diastolic blood pressure. miRNA-92a-3p partially mediates the correlation between noise exposure and blood pressure (13). miRNA-126 and HIF-1$\alpha$ expression in patients with hypertension associated with obstructive sleep apnea-hypopnea syndrome was explored, and it was found that patients with hypertension associated with obstructive sleep apnea-hypopnea syndrome had lower levels of miRNA-126 than the controls (4).

*Correlation between the inflammatory factor IL-6 and miRNAs expression*

miRNA-21 expression showed a positive correlation with IL-6, whereas miRNA-92a and miRNA-126 exhibited negative correlations (*Figure 3*). After surgical trauma, IL-6 tends to increase rapidly, reflecting the overall inflammatory state. It regulates the expression of various miRNAs by activating signaling pathways such as JAK/STAT and NF-κB. The upregulation of miRNA-21 has been widely confirmed to be closely related to inflammatory stimulation. Its expression in vascular smooth muscle cells and macrophages can be induced by IL-6, which, in turn, promotes cell proliferation and inhibits apoptosis, forming an »inflammation-remodeling« positive feedback

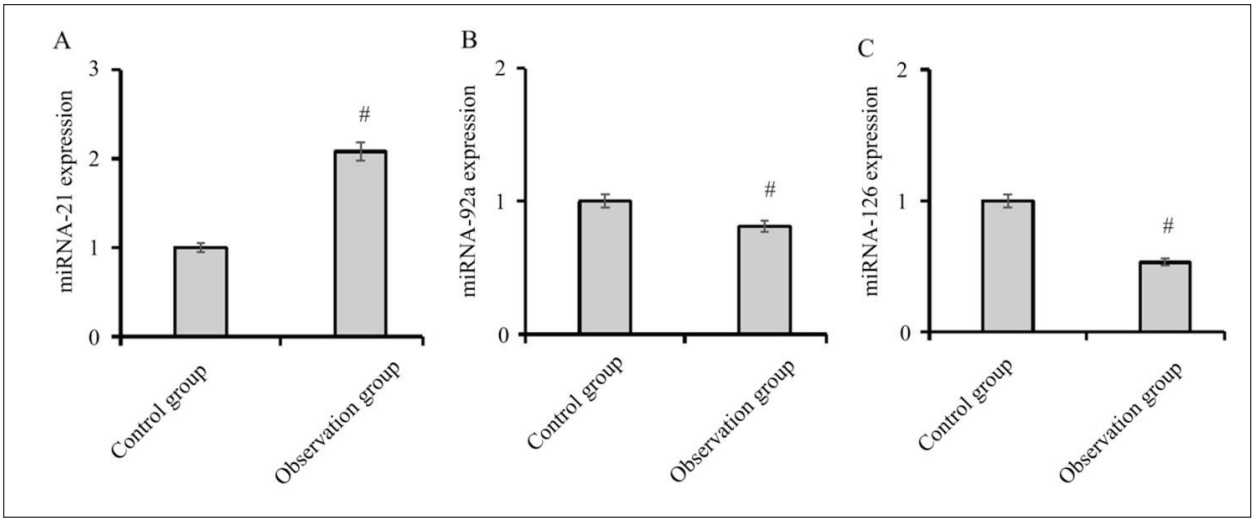


**Figure 2** Analysis of miRNAs expression.
Note: (A) miRNA-21; (B) miRNA-92a; (C) miRNA-126. #relative to the BG, $P < 0.05$

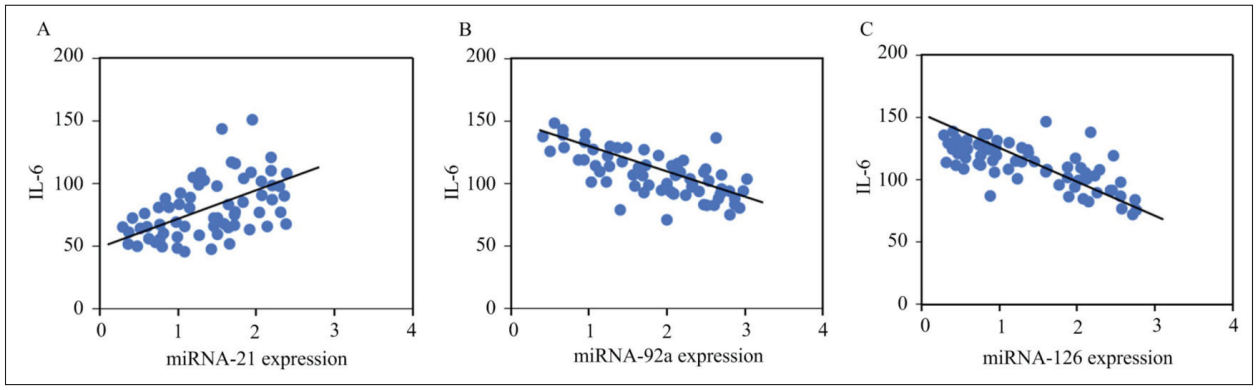


**Figure 3** Correlation between inflammatory factor IL-6 and miRNAs expression.
Note: (A) IL-6 and miRNA-21; (B) IL-6 and miRNA-92a; (C) IL-6 and miRNA-126

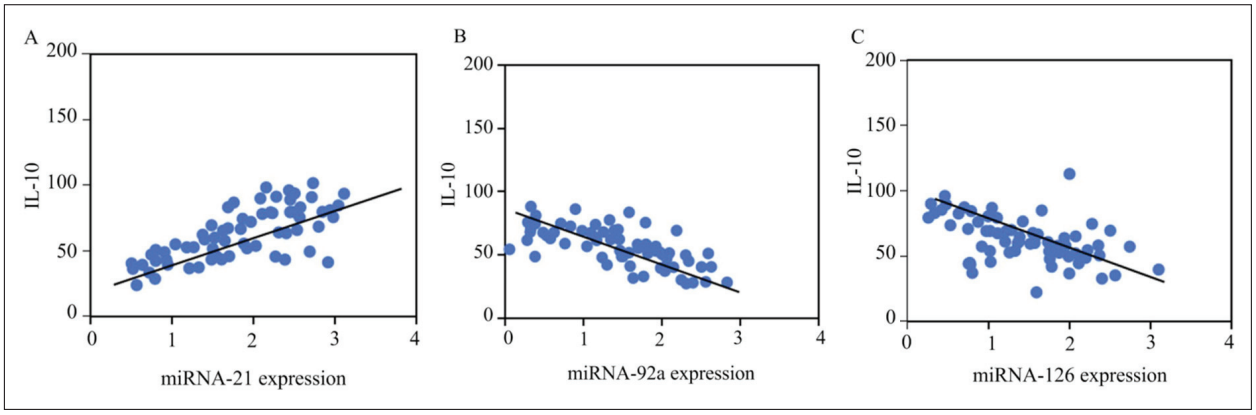


**Figure 4** Correlation between inflammatory factor IL-10 and miRNAs expression.
Note: (A) IL-10 and miRNA-21; (B) IL-10 and miRNA-92a; (C) IL-10 and miRNA-126

loop. This is an adaptive response of the body to vascular injury. As an important protective factor for endothelial function, miRNA-126 expression is typically inhibited in an inflammatory environment. The increase in IL-6 may indirectly inhibit miRNA-126 production by down-regulating KLF2 or ETS family transcription factors, leading to reduced endothelial repair capacity and increased expression of adhesion molecules, thereby exacerbating endothelial dysfunction. This study indicated the presence of a complex regulatory network during the acute phase of PCI. Under high-inflammation conditions, miRNA-92a may be feedback-regulated downward. Research has highlighted the significance of interaction between cytokines and miRNAs across several neurological conditions, aiming to uncover novel mechanistic insights and biomarker candidates relevant to disease progression and diagnosis (14). A significant positive correlation was noted (miRNA-155 and TNF-α, miRNA-182 and CCL2). The GO-antisense miRNA-21 complex can more forcefully regulate the expression of a variety of key cytokines (15): The gene and protein expression of TIMP-2 was evidently elevated in U87, U251, and T98 cells; The protein expression of ICAM-1 was down-regulated in all four cell lines; The mRNA and protein levels of IL-8 were also obviously reduced.

*Correlation between the inflammatory factor IL-10 and miRNAs expression*

miRNA-21 expressionshowed a positive correlation with IL-10, whereas miRNA-92a and miRNA-126 exhibited negative correlations (*Figure 4*). As a classical anti-inflammatory cytokine, IL-10 is usually secreted by regulatory T cells and M2 macrophages in the late stage of inflammation to suppress excessive inflammatory responses and promote tissue repair. The increase in IL-10 indicates a shift toward an anti-inflammatory, repair state. In this study, the negative correlation between IL-10 and miRNA-126 suggested that within a specific time window after PCI, the increase in IL-10 may not simply reflect a protective anti-inflammatory state, but rather a complex response associated

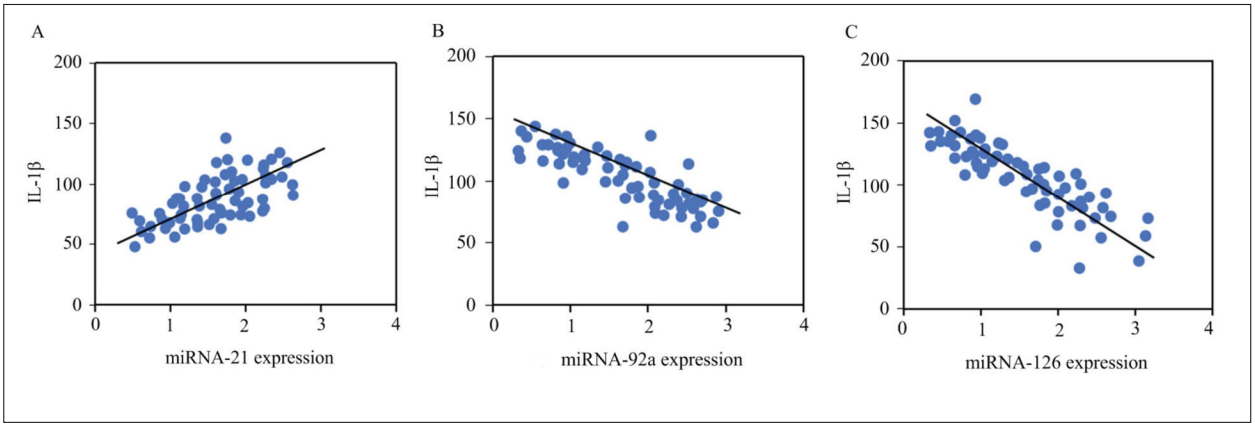


**Figure 5** Correlation between inflammatory factor IL-1β and miRNAs expression.
Note: (A) IL-1β and miRNA-21; (B) IL-1β and miRNA-92a; (C) IL-1β and miRNA-126

with tissue damage and cellular stress. miRNA-21 not only promotes the multiplication of smooth muscle cells, but also participates in the regulation of immune tolerance and anti-inflammatory phenotype formation in T cells and macrophages; it can negatively regulate the NF-κB pathway by targeting PDCD4, thereby promoting the production of IL-10 and forming a »miRNA-21 → IL-10 → anti-inflammatory« positive feedback loop. The negative correlation between miRNA-92a, miRNA-126, and IL-10 indicated that stronger signals inhibited their expression. For example, acute endothelial injury caused by PCI may evidently downregulate miRNA-126, which cannot be restored even in the context of increased IL-10. miRNA-92a has different functions at different pathological stages. Its downregulation in the late stage of inflammation may be due to negative feedback or changes in cell sources. miRNA particles are involved in regulating atherosclerotic plaque instability (16). The study revealed that miR-10b and miR-92a regulated KLF4 and KLF2 in patients with more vulnerable plaque phenotypes. Targeting miRNA-92a in VSMC with a KLF4 inhibitor suppressed the synthetic phenotype and VSMC multiplication and transfer, while reducing KLF4 expression, suggesting that miR-92a may indirectly reduce IL-10 production by inhibiting KLF4 (5).

*Correlation between the inflammatory factor IL-1β and miRNAs expression*

miRNA-21 expression suggested a positive correlation with IL-1β, while miRNA-92a and miRNA-126 exhibited negative correlations (*Figure 5*). As a key effector activated after NLRP3 inflammasome activation, IL-1β is rapidly induced during PCI by mechanical vascular endothelial injury, oxidative stress, and cholesterol crystal release, driving local inflammatory responses and altering the transcriptional regulation of various miRNAs through signaling pathways such as NF-κB and MAPK. miRNA-21, an important molecule responding to inflammatory stimuli, can be up-regulated by IL-1β, promoting smooth muscle cell proliferation and migration by inhibiting target genes such as PTEN and Sprouty1, and contributing to neointimal formation. Therefore, the two are positively correlated. The higher the level of IL-1β, the stronger the repair and potentially stenosis-inducing response mediated by miRNA-21. miRNA-126 expression is influenced by endothelial cells. In a sustained inflammatory environment, IL-1β can down-regulate endothelial protective transcription factors such as KLF2 and ERK5, thereby inhibiting miRNA-126 production, reducing its expression, and weakening vascular repair capacity, promoting leukocyte adhesion, and causing endothelial dysfunction. In this study, the negative correlation between miRNA-92a and IL-1β indicated that in the acute phase of PCI, with strong inflammatory stimulation, miRNA-92a was feedback-regulated downward. CAD-related miRNAs targeting differentially expressed genes include hsa-miR-206, has-miR-320b, etc. (17). hsa-miR-92a-3p regulates the most differentially expressed genes. IL-1β is a key inflammatory mediator in CAD, suggesting a possible negative feedback regulation between the two. Administration of miRNA-214-5p agomiR can reverse the improvement in psoralen-treated lipopolysaccharide-treated mouse cardiac function and the elevation of IL-1β, IL-6, and TNF-α (18). Psoralen improves sepsis-related cardiac dysfunction by suppressing the inflammatory response. Psoralen reduces miRNA-214-5p to in-hibit the sepsis inflammatory response.

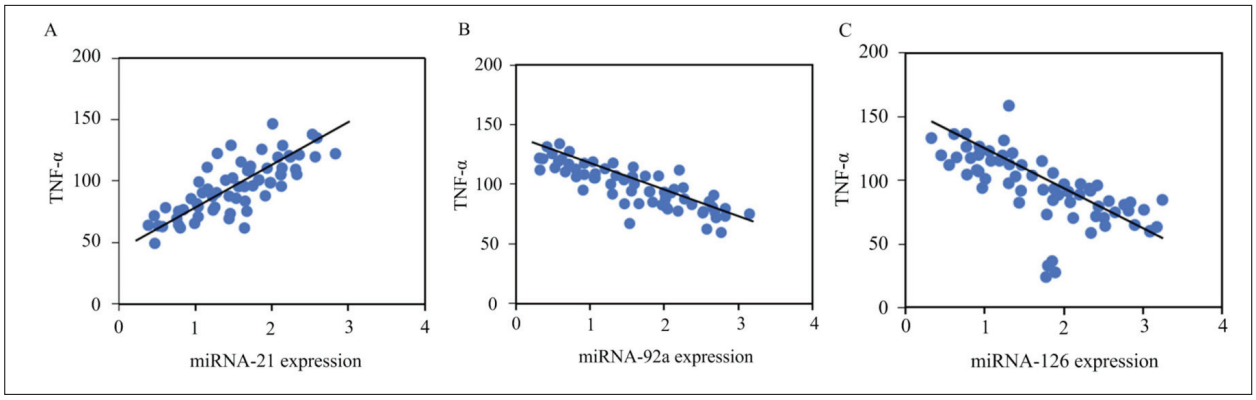


**Figure 6** Correlation between inflammatory factor TNF-α and miRNAs expression.
Note: (A) TNF-α and miRNA-21; (B) TNF-α and miRNA-92a; (C) TNF-α and miRNA-126

*Correlation between the inflammatory factor TNF-α and miRNAs expression*

miRNA-21 expression suggested a positive correlation with TNF-α, while miRNA-92a and miRNA-126 exhibited negative correlations (*Figure 6*). TNF-α treatment down-regulates miR-27b expression in all endothelial cell lines, thereby activating inflammatory pathways, inducing mitochondrial alterations and reactive oxygen species accumulation, and promoting intrinsic apoptosis (2).

## Discussion

The findings of this study provide new insights into the dynamic interplay between inflammatory cytokines and specific miRNAs in patients undergoing PCI. Our results demonstrate that PCI not only induces a significant systemic inflammatory response, characterized by elevated levels of IL-6, IL-10, IL-1β, and TNF-α, but also modulates the expression of key miRNAs involved in vascular homeostasis and repair. The upregulation of miRNA-21 and the downregulation of miRNA-92a and miRNA-126 reflect a coordinated molecular response to vascular injury, with significant correlations suggesting a regulatory network linking inflammation and vascular remodeling.

The observed increase in pro-inflammatory cytokines (IL-6, IL-1β, TNF-α) aligns with previous reports highlighting PCI as a potent trigger of systemic inflammation, largely due to mechanical endothelial injury, plaque disruption, and stent-induced foreign body reactions (9, 10). Notably, the concurrent rise in IL-10, an anti-inflammatory cytokine, suggests a compensatory regulatory attempt to mitigate excessive inflammation. However, the overall cytokine profile indicates a pro-inflammatory predominance, which may contribute to endothelial dysfunction, plaque instability, and adverse cardiovascular outcomes if not adequately regulated (11).

At the miRNA level, miRNA-21 emerged as a central player, showing significant up-regulation and positive correlation with all measured inflammatory factors. miRNA-21 is known to promote vascular smooth muscle cell proliferation, inhibit apoptosis, and enhance inflammatory signaling through pathways such as NF-κB and JAK/STAT (15). Its elevation post-PCI may therefore represent an adaptive reparative response. Yet, persistent overexpression could predispose to neointimal hyperplasia and in-stent restenosis, highlighting its dual role in vascular healing and pathology.

Conversely, miRNA-92a and miRNA-126 were significantly down-regulated post-PCI. Both miRNAs are recognized as endothelial-protective factors. miRNA-126, in particular, supports endothelial integrity, angiogenesis, and anti-inflammatory responses via VEGF and PI3K/Akt signaling (4). Its suppression in our study likely reflects endothelial damage sustained during PCI, impairing vascular repair capacity. Similarly, reduced miRNA-92a expression may be linked to endothelial dysfunction and negative feedback regulation under inflammatory stress, consistent with findings that miRNA-92a inhibition attenuates smooth muscle cell proliferation and mitigates restenosis (5).

The strong correlations between cytokine levels and miRNA expression patterns suggest an »inflammation-miRNA axis« that orchestrates vascular responses post-PCI. For instance, IL-6 and TNF-α may drive miRNA-21 upregulation while suppressing miRNA-126, thereby shifting the balance toward inflammation and remodeling. IL-10, despite its anti-inflammatory role, showed negative correlations with protective miRNAs, possibly indicating a complex feedback mechanism or temporal dissociation between cytokine release and miRNA regulation.

These interactions may have important clinical implications. miRNAs such as miRNA-21, miRNA-

92a, and miRNA-126 could serve as biomarkers for monitoring post-PCI vascular inflammation and repair. Furthermore, therapeutic modulation of these miRNAs – for example, using antagomiRs or mimetics – might offer novel strategies to enhance endothelial recovery, reduce restenosis, and improve long-term outcomes after PCI. Recent studies have already explored miRNA-based interventions in cardiovascular contexts, supporting their translational potential (8, 14). Several limitations of this study should be acknowledged. First, our analysis was restricted to a single postoperative time point (72 hours), thereby failing to capture the dynamic evolution of inflammatory and miRNA responses over time. Second, the sample size was relatively small, and all participants were from a single center, which may limit generalizability. Third, while correlations were identified, causal relationships between cytokines and miRNAs remain to be established through functional studies (19, 20).

Future research should include longitudinal sampling to delineate the time course of inflammatory and miRNA changes before, during, and after PCI. Larger multi-center cohorts and integration with clinical outcome data will help validate the prognostic value of these biomarkers. Mechanistic studies using in vitro and animal models are also needed to elucidate the precise pathways through which miRNAs modulate post-PCI vascular biology.

In conclusion, this study reveals a coordinated response involving inflammatory cytokines and regulatory miRNAs in patients undergoing PCI. These findings underscore the potential of miRNAs as biomarkers and therapeutic targets in the management of post-PCI vascular repair and remodeling. Further exploration of the inflammation-miRNA axis may pave the way for personalized approaches to improve cardiovascular outcomes after interventional procedures.

## Conclusion

The correlation between inflammatory factors and the expression of specific miRNAs in patients undergoing PCI was systematically revealed. The results indicated that IL-6, IL-1β, TNF-α, and IL-10 in the serum of patients after PCI were significantly elevated, with up-regulated plasma miRNA-21 and down-regulated miRNA-92a and miRNA-126. Correlation analysis found that the levels of inflammatory factors were positively correlated with miRNA-21 and negatively correlated with miRNA-92a and miRNA-126. It suggested that, in the complex vascular biological response after PCI, there was an »inflammation-remodeling« axis composed of inflammatory signals and miRNA regulatory networks, which jointly contributed to vascular endothelial injury. The limitation of this study is that only indicators at 3 days after surgery are analyzed, without examining the full time course of inflammation and miRNA dynamics. In the future, changes in the spectra of inflammatory factors and miRNAs at multiple time points (before, during, and after PCI) should be dynamically monitored, and the clinical potential of diagnostic tools or therapeutic drugs targeting these miRNAs in the perioperative management of PCI should be explored.

*Authors' contribution*

Chuanwen Jiang and Xiaojun Zhou contributed equally to this work and are co-first authors. All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Chuanwen Jiang, Xiaojun Zhou, Qidong Cao, and Linchun Cao. The first draft of the manuscript was written by Juan Zhang and Xiaolong Qin, with Shuai Zeng, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

## Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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