Cerrahpaşa Med J 2024; 48(3): 294-297 ORIGINAL ARTICLE

Investigation of the Role of Molecules in DNA Repair Process in Coronary Artery Patients

Narmina Malikova[1], Murat Cimci[2], Damla Raimoglou[2], Ahmet Özaydın[2], Eser Durmaz[2], Barış İkitimur[2], Bilgehan Karadağ[2], Mehmet Güven[1]

[1]Department of Medical Biology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Türkiye
[2]Department of Cardiology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Türkiye

Cite this article as: Malikova N, Cimci M, Raimoglou D, et al. Investigation of the role of molecules in DNA repair process in coronary artery patients. *Cerrahpaşa Med J*. 2024;48(3):294-297.

Abstract

Objective: The role of DNA damage in the progression of coronary artery disease (CAD) is widely recognized. Among the factors that determine the extent of DNA damage, genetic factors may be one of the determining factors in the pathogenesis of CAD.

Methods: In our research, we investigated the expression levels of *BRCA1* and *PARP1*, which are involved in the DNA repair process, as well as the regulators of gene expression for these molecules, namely *miR-21-5p*, *miR-193b-3p*, and *miR-484*, in lymphocyte samples collected from 55 patients with CAD and 55 healthy controls.

Results: The fold changes of *BRCA1, PARP1, miR-21-5p, miR-193b-3p* and *miR-484* expression levels in the patient group, as determined by the $2^{-\Delta\Delta CT}$ calculation, were found to be 0.353, 0.332, 0.734, 0.876, and 1.231, respectively. In the patient group, a statistically significant negative correlation was observed only between *PARP1* and *miR-21* ($r = -0.66$, $P = .0001$).

Conclusion: The expression levels in molecules related to the DNA repair systems of CAD patients are clearly related to the pathogenesis of the disease, and considering this situation, measures to be taken would be beneficial.

Keywords: Coronary artery disease, BRCA1, PARP1, miR-21-5p, miR-193b-3p, miR-484

Introduction

Coronary artery disease (CAD) was defined as documentation of CAD with stable anginal symptoms and/or dyspnea according to the latest European Society of Cardiology Chronic Coronary Syndrome guidelines.[1] It is known that DNA damages contribute to the pathogenesis of this disease. Generally, these damages are in the form of single base mutations, chain breaks, base deletions, or base modifications.[2] The role of DNA repair mechanisms is very important in maintaining genomic integrity. Different DNA repair mechanisms exist for the repair of different DNA damages in mammalian cells.

BRCA1 serves as a key susceptibility gene for breast and ovarian cancer.[3] It consists of several domains that are essential for upholding genomic stability, such as DNA repair, DNA damage signaling, chromatin remodeling, regulation of cell cycle checkpoints, protein ubiquitination, transcriptional regulation, and apoptosis. By regulating homologous recombination (HR), the BRCA1 protein plays a crucial role in the process of DNA double-strand break repair.[4]

PARP1 is an essential ADP-ribosylating enzyme that plays a crucial role in initiating multiple cellular processes, including DNA repair, regulation of cell cycle progression, preservation of telomeres, modulation of chromatin structure, and resolution of replicative stress.[5] This activity of PARP1 contributes to DNA repair, including the repair of double-strand breaks and single-strand breaks. PARP1 participates in various pathways responsible for DNA repair, including nucleotide excision repair (NER), non-homologous end-joining, HR, and base excision repair.[6]

MicroRNAs (miRNAs) are non-coding 20-24 nucleotide small RNAs and are master regulators of the cellular system. MicroRNAs regulate multiple target genes at the post-transcriptional level in eukaryotic gene expression regulation. miR-484 has garnered recognition as a pivotal controller influencing not only cancer but also a range of diseases or pathological conditions.[7] miR-484 is most abundantly expressed in the heart tissue. Extensive evidence has substantiated the potential intimate association between miR-484 and diseases related to cardiac ischemia.[7] In the breast cancer study, BRCA1 was also identified as interacting with miR-484.[8] Partaking in numerous physiological and pathological processes, miR-193b-3p, positioned at 16p13, assumes a significant role as a regulatory factor. Multiple studies have recently provided evidence that miR-193b, a known tumor suppressor, is commonly downregulated in different cancer types.[9] In various studies, it has also been shown that the miR-193 family plays a role in the pathological processes underlying cardiovascular disorders.[11] It has been reported that miR-193b-3p is among the targets of PAPR1.[12] miR-21-5p is highly expressed in the cardiovascular system. Several studies have suggested that miR-21-5p expression in the heart is dysregulated under cardiovascular diseases such as calcific aortic valve disease, cardiac hypertrophy, and ischemic heart disease or heart failure.[11] PARP1 has been recognized as a direct target of miR-21–5p.[13]

Received: August 2, 2024 **Revision requested:** September 19, 2024
Last revision received: September 23, 2024 **Accepted:** November 20, 2024
Publication Date: December 18, 2024
Corresponding author: Mehmet Güven, Department of Medical Biology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Türkiye
e-mail: mguven@iuc.edu.tr; mguven66@gmail.com
DOI: 10.5152/cjm.2024.24039

In our study, we examined the gene expression levels of *BRCA1* and *PARP1*, which are involved in the DNA damage repair mechanism, and microRNAs (*miR-21-5p, miR-193b-3p* and *miR-484*), which play a role in the regulation of gene expression of these molecules in blood samples of patients diagnosed with CAD and healthy controls.

Methods

Fifty-five randomly selected patients who needed coronary angiography due to a history or symptoms of CAD were included in the study. The presence of CAD was determined by coronary angiography in the catheterization laboratory of the Cardiology Department of İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine using the standard catheterization technique.

The exclusion criteria of our study included being younger than 18 years of age, a history of prior coronary revascularization, recent clinical infection, myocardial infarction within 30 days, unstable angina, and concurrent major hepatic, renal, immunological, inflammatory, and neoplastic disease. Data including cardiovascular risk factors such as smoking habits, diabetes, family history, and hypertension were obtained from all individuals participating in the study. None of the individuals in the study had taken antioxidant therapy in the previous month. Fifty-five healthy individuals matched with the patients in terms of gender, age, and cardiovascular risk factors were used as the control group. They were evaluated as healthy based on clinical examination and family history of CAD. All participants in the study provided written informed consent as a prerequisite. The study protocol was approved by the İstanbul University Cerrahpaşa, Cerrahpaşa Faculty of Medicine (Approval no: 71759/08.10.2018, Date: September 21, 2018). Prior to the angiographic procedure, blood samples were taken from the patients. The demographic and clinical characteristics of the patients and controls have been included as Table 1 in our revised article.

Reverse Transcription-Quantitative Polymerase Chain Reaction

Reverse transcription-quantitative polymerase chain reaction was employed to examine the expression levels of the investigated genes. Total RNA extracted from lymphocyte samples of both patients and controls was utilized for this analysis.[14] The gene expression studies were conducted in triplicate for each sample.

Statistical Analysis

Mean ± standard error (SE) or mean ± standard deviation (SD) was used to present continuous parametric data. For the statistical analysis of continuous variables, the *t*-test and Mann–Whitney *U*-test were employed. The chi-squared test (χ^2 test) and Fisher's exact test were used to compare categorical data, which were presented as counts and percentages. To determine the correlation, Pearson correlation analysis was utilized, and a statistical significance level of $P < .05$ was considered acceptable.

Table 1. Demographic and Clinical Parameters for Patients and Controls

	Patients	Controls
Total	55	55
Age (years)	64 ± 8	62 ± 7
Gender (n)		
Female	30	25
Male	25	30
Diabetic patients (n)	20	
Hypertensive patients (n)	25	
Smokers (n)	13	

Results

The $2^{-\Delta\Delta CT}$ values of the *PARP1*, *BRCA1*, *miR-21-5p*, *miR-193b-3p,* and *miR-484* genes of the patient and control groups were calculated. As seen in Table 2, there was no difference in gene expression levels between the patient and control groups according to the $2^{-\Delta\Delta CT}$ calculation.

According to the $2^{-\Delta\Delta CT}$ calculation of the results, *BRCA1*, *PARP1*, *miR-21-5p*, and *miR-193b-3p* expression levels in the patient group were found to be fold decreased (0.353, 0.332, 0.734, 0.876, respectively) when compared to the control group. On the other hand, *miR-484* expression levels in the patient group were found to be 1.231 fold when compared to the control group.

In our study, we examined the relationship between *BRCA1* gene expression levels and *miR-484* expression levels, and between *PARP1* gene expression levels and *miR-21-5p* and *miR-193b-3p* expression levels in the patient and control groups. A statistically significant negative correlation was found only between *PARP1* and *miR-21* in the patient group ($r = -0.66$, $P = .0001$). In the control group, a statistically significant negative correlation was found only between *BRCA1* and *miR-484* ($r = -0.35$, $P = .05$).

Discussion

Studies in chronic heart diseases have reported that reactive oxygen species increases and this leads to DNA damage. It has been stated that deficiencies in endogenous DNA damage repair in cardiomyocytes may lead to insufficiency in maintaining normal cardiac functions and thus may lead to the early onset of heart failure.[15] It has been shown that low expression of some DNA repair genes, such as *ATM*, *XPA*, and *ERCC1*, is associated with myocardial infarction.[16] However, the importance of DNA damage repair failure in the pathogenesis of heart diseases has not been fully elucidated. In our study, we investigated the *PARP1* and *BRCA1* genes that play a role in the repair of DNA damage and the miRNAs that regulate the expression levels of these genes.

Activation of PARP1, a DNA damage sensor, causes a decrease in NAD and ATP levels. In studies with animal models, moderate PARP1 activation increases were associated with DNA repair. On the other hand, excessive realization of this energy-consuming process can lead to cell dysfunction, cell death, and thus various pathologies.[17] Numerous investigations have demonstrated the significant involvement of the PARP1 enzyme in the development of

Table 2. Gene Expression Levels of Patient and Control Groups

	Patients	Controls	*P*
miR-193b-3p	0.088 ± 0.033	0.119 ± 0.035	.52*
miR-21-5p	0.094 ± 0.031	0,164 ± 0.037	.16*
miR-484	0.304 ± 0.041	0.347 ± 0.044	.48*
PARP1	0.018 ± 0.008	0.065 ± 0.027	.41**
BRCA1	0.095 ± 0.032	0.032 ± 0.006	.61**

*Student *t*-test.
**Mann–Whitney *U*-test.

diverse cardiovascular conditions, including hypertension, heart failure, cardiomyopathies, myocardial infarction, ischemia-reperfusion injury, and myocardial hypertrophy.[18] Hans et al[19] reported that PARP1 protein activity is increased in atherosclerotic plaque and that *PARP1* gene deletion in mice regresses the formation of atherosclerotic plaques. It has been reported in various studies that *PARP1* overexpression causes cardiac dysfunction and that these pathologies can be prevented by PARP1 inhibition.[20] Although studies have been conducted on high PARP1 enzyme levels in cardiovascular diseases, the negative effects of this situation, and the effect of PARP1 enzyme inhibitors, no study has been found on *PARP1* gene expression level in CAD patients. In our study, we did not detect a significant change in *PARP1* expression level in CAD patients. The lack of a complete relationship between gene expression level and protein level due to post-transcriptional modifications may be the reason why *PARP1* gene expression level was detected at normal levels in our study. On the other hand, it can also show that the *PARP1* expression level in CAD is within normal limits; thus, the DNA damage level is not excessively increased.

Apart from the association of *BRCA1* mutations with various types of cancer, BRCA1 is likely to play a role in the pathogenesis of many chronic diseases other than cancer due to its role in the DNA repair mechanism. Therefore, *BRCA1* mutation carriers may carry a risk for cardiovascular diseases. It has been shown that *BRCA1* mutations cause cardiovascular complications rather than cancer, especially in the elderly.[21] Studies showing the relationship between *BRCA1* gene polymorphisms and myocardial infarction also reveal the importance of BRCA1 in terms of cardiac functions.[22] In a study by Shukla et al,[23] they showed that loss of BRCA1 function in cardiomyocytes in mice resulted in increased double-strand DNA breaks, apoptosis, and ultimately led to cardiac failure. There are studies showing that *BRCA1* and *BRCA2* mutations cause cardiovascular disorders through apoptosis in cardiomyocytes via the p53 pathway.[24] On the other hand, there are also studies showing that there is no relationship between being a carrier of *BRCA1/2* mutations and cardiomyopathy.[25] In our research, we observed no notable disparity in *BRCA1* gene expression levels between the CAD group and the control group. There was no study in our patient group that would compare our results. Although the relationship between *BRCA1* mutations and cardiovascular diseases has been emphasized in the literature, no results related to gene expression changes have been reported.

The results of the study showing the relationships between various pathological conditions related to the heart and miRNA profiles led them to be evaluated as potential diagnostic and prognostic markers. In our research, we examined the levels of expression of three specific miRNAs (*miR-484*, *miR-21-5p*, and *miR-193b-3p*). These miRNAs act as regulators of gene expression, influencing the levels of molecules involved in the development of CAH and heart diseases.

Although it has been shown that *BRCA1* interacts with *miR-484*, it has been reported that this interaction does not cause any change in *BRCA1* expression level.[8] While no correlation was found between these 2 molecules in the patient group in our study, an inverse relationship was found at the borderline significance level in the control group. One of the organs in which *miR-484* is most expressed is the heart, and disruptions in *miR-484* expression have been shown to be associated with cardiac ischemia.[7] Su et al[26] showed that the expression level of *miR-484* was significantly altered in heart failure. In a study conducted with CAD patients, the miR-484 level was found to be higher than in healthy individuals.[27] Gongol et al[28] showed that the level of miR-484 increased in the serum of CAD patients and reported that miR-484 may be important in endothelial dysfunction and therefore in the pathogenesis of cardiovascular diseases. In our study, no change was detected in the lymphocyte miR-484 level in CAD patients compared with controls. On the other hand, Masoodi Khabar et al[29] found increased expression level of miR-484 in platelets of patients with acute coronary syndrome. The study participants encompassed individuals diagnosed with acute myocardial infarction (AMI) characterized by ST-segment elevation), unstable angina (UA), and non-ST-elevation AMI. Different cell types and different patient groups may be the reason for the difference in the results of the studies. There are many studies in the literature that miR-193b-3p is associated with tumor progression and inflammation.[10,30] On the other hand, there are many studies examining the status of this miRNA in cardiovascular diseases. Wong et al[31] determined that the plasma miR-193b-3p level was high in patients with heart failure. In a study by Bai et al[32] investigating the role of miR-193b-3p in patients with atherosclerosis, they found that the serum miR-193b-3p level of the patients was lower than the control group. They also determined that inhibition of miR-193b-3p led to the reduction of damage induced by ox-LDL. In a study investigating the link between miR-193b-3p and myocardial ischemia-reperfusion injury, researchers observed a decrease in the expression level of miR-193b-3p in cases involving myocardial ischemia-reperfusion injury. In this study, it was also determined that an increase in *miR-193b-3p* expression levels reduces apoptosis after myocardial ischemia-reperfusion injury.[33] In our study, we found that the expression level of *miR-193b-3p* in CAD patients was at a normal level. The differences between the results may be due to the differences in the patient groups and the material studied.

There are studies showing that the expression level of *miR-21-5p* increases in the regulation of expression levels of proteins associated with compensatory mechanisms such as reduction of apoptosis and maintenance of survival in case of damage to cardiomyocytes. It was stated that miR-21-5p was high in the plasma of patients with heart failure and its level did not vary with age and gender.[34] In a study conducted in arteria mammaria interna samples of patients with CAD, it was determined that the expression level of *miR-21-5p* was correlated with chronic obstructive pulmonary disease, one of the risk factors for CAD.[35] In a study by Patterson et al,[36] when Patterson et al[36] compared the CAD group with a low Framingham risk score and the non-CAD group with a low Framingham risk score in peripheral blood samples, no difference was found in *miR-21-5p* expression as in our study.

One major limitation of this study is the small sample size, which may reduce the statistical strength of our analyses. Therefore, further research involving a larger sample is needed to confirm these results.

Although no differences were detected in the expression levels of DNA repair enzyme genes in CAD patients, we demonstrated that the miRNAs we studied regulate the expression of these DNA repair enzymes, which are their targets.

Availability of Data and Materials: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İstanbul University Cerrahpaşa, Cerrahpaşa Faculty of Medicine (Approval no: 71759/08.10.2018, Date: September 21, 2018).

Informed Consent: Written informed consent was obtained from all participants in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.G., B.K.; Design – M.G.; Supervision – B.I., E.D., A.O.; Materials – D.R., M.C.; Data Collection and/or Processing – N.M.; Analysis and/or Interpretation – N.M., M.G., A.O.; Literature Review – M.Ç., D.R.; Writing – M.G.; Critical Review – M.G., B.K.

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

Funding: This work was supported by the Research Fund of İstanbul University-Cerrahpaşa (Grant no: 31550).

References

1. Vrints C, et al. ESC Guidelines on the management of chronic coronary syndromes. *Eur Heart J*. 2024:ehae177.
2. Heimlich JB, Bick AG. Somatic mutations in cardiovascular disease. *Circ Res*. 2022;130(1):149-161. [CrossRef]
3. Xu J, Wang B, Zhang Y, Li R, Wang Y, Zhang S. Clinical implications for BRCA gene mutation in breast cancer. *Mol Biol Rep*. 2012;39(3):3097-3102. [CrossRef]
4. Xu Y, Xu D. Repair pathway choice for double-strand breaks. *Essays Biochem*. 2020;64(5):765-777. [CrossRef]
5. Molinaro C, Martoriati A, Cailliau K. Proteins from the DNA damage response: regulation, dysfunction, and anticancer strategies. *Cancers (Basel)*. 2021;13(15):3819. [CrossRef]
6. Spiegel JO, Van Houten B, Durrant JD. PARP1: structural insights and pharmacological targets for inhibition. *DNA Repair (Amst)*. 2021;103:103125. [CrossRef]
7. Jia YZ, Liu J, Wang GQ, Song ZF. miR-484: A potential biomarker in health and disease. *Front Oncol*. 2022;12:830420. [CrossRef]
8. Volinia S, Croce CM. Prognostic microRNA/mRNA signature from the integrated analysis of patients with invasive breast cancer. *Proc Natl Acad Sci U S A*. 2013;110(18):7413-7417. [CrossRef]
9. Bhayadia R, Krowiorz K, Haetscher N, et al. Endogenous tumor suppressor microRNA-193b: therapeutic and prognostic value in acute myeloid leukemia. *J Clin Oncol*. 2018;36(10):1007-1016. [CrossRef]
10. Chen Z, Yang J, Zhong J, et al. MicroRNA-193b-3p alleviates focal cerebral ischemia and reperfusioninduced injury in rats by inhibiting 5-lipoxygenase expression. *Exp Neurol*. 2020;327:113223. [CrossRef]
11. Petkova V, Marinova D, Kyurkchiyan S, et al. MiRNA expression profiling in adenocarcinoma and squamous cell lung carcinoma reveals both common and specific deregulated microRNAs. *Med (Baltim)*. 2022;101(33):e30027. [CrossRef]
12. Xu L, Tian L, Yan Z, Wang J, Xue T, Sun Q. Diagnostic and prognostic value of miR-486-5p, miR-451a, miR-21-5p and monocyte to high-density lipoprotein cholesterol ratio in patients with acute myocardial infarction. *Heart Vessels*. 2023;38(3):318-331. [CrossRef]
13. Sun P, Zhang S, Wu D, Qian Y, Xiao X, Zhang Q. MiR-21 modulates proliferation and apoptosis of human airway smooth muscle cells by regulating autophagy via PARP-1/AMPK/mTOR signalling pathway. *Respir Physiol Neurobiol*. 2022;301:103891. [CrossRef]
14. Mutlu T, Ozoran E, Trabulus DC, et al. Expression of genes related to iron homeostasis in breast cancer. *Mol Biol Rep*. 2023;50(6):5157-5163. [CrossRef]
15. Higo T, Naito AT, Sumida T, et al. DNA single-strand break-induced DNA damage response causes heart failure. *Nat Commun*. 2017;8:15104. [CrossRef]
16. Zhang S, Wang XB, Han YD, et al. Polymorphism in ERCC1 confers susceptibility of coronary artery disease and severity of coronary artery atherosclerosis in a Chinese Han population. *Sci Rep*. 2017;7(1):6407. [CrossRef]
17. Wang J, Hao L, Wang Y, et al. Inhibition of poly (ADP-ribose) polymerase and inducible nitric oxide synthase protects against ischemic myocardial damage by reduction of apoptosis. *Mol Med Rep*. 2015;11(3):1768-1776. [CrossRef]
18. Henning RJ, Bourgeois M, Harbison RD. Poly(ADP-ribose) polymerase (PARP) and PARP inhibitors: mechanisms of action and role in cardiovascular disorders. *Cardiovasc Toxicol*. 2018;18(6):493-506. [CrossRef]
19. Hans CP, Zerfaoui M, Naura AS, Catling A, Boulares AH. Differential effects of PARP inhibition on vascular cell survival and ACAT-1 expression favouring atherosclerotic plaque stability. *Cardiovasc Res*. 2008;78(3):429-439. [CrossRef]
20. Martinet W, Knaapen MW, De Meyer GR, Herman AG, Kockx MM. Elevated levels of oxidative DNA damage and DNA repair enzymes in human atherosclerotic plaques. *Circulation* 2002;106: 927-32. (https://doi: 10.1161/01.cir.0000026393.47805.21)
21. Bordeleau L, Lipscombe L, Lubinski J, et al. Diabetes and breast cancer among women with BRCA1 and BRCA2 mutations. *Cancer*. 2011;117(9):1812-1818. [CrossRef]
22. Ozaki K, Sato H, Inoue K, et al. SNPs in BRAP associated with risk of myocardial infarction in Asian populations. *Nat Genet*. 2009;41(3):329-333. [CrossRef]
23. Shukla PC, Singh KK, Quan A, et al. BRCA1 is an essential regulator of heart function and survival following myocardial infarction. *Nat Commun*. 2011;2:593. [CrossRef]
24. Barac A, Lynce F, Smith KL, et al. Cardiac function in BRCA1/2 mutation carriers with history of breast cancer treated with anthracyclines. *Breast Cancer Res Treat*. 2016;155(2):285-293. [CrossRef]
25. Pearson EJ, Nair A, Daoud Y, Blum JL. The incidence of cardiomyopathy in BRCA1 and BRCA2 mutation carriers after anthracycline-based adjuvant chemotherapy. *Breast Cancer Res Treat*. 2017;162(1):59-67. [CrossRef]
26. Su Y, Sun Y, Tang Y, et al. Circulating miR-19b-3p as a novel prognostic biomarker for acute heart failure. *J Am Heart Assoc*. 2021;10(20):e022304. [CrossRef]
27. Wang HW, Lo HH, Chiu YL, et al. Dysregulated miR-361-5p/VEGF axis in the plasma and endothelial progenitor cells of patients with coronary artery disease. *PLOS ONE*. 2014;9(5):e98070. [CrossRef]
28. Gongol B, Marin T, Zhang J, et al. Shear stress regulation of miR-93 and miR-484 maturation through nucleolin. *Proc Natl Acad Sci U S A*. 2019;116(26):12974-12979. [CrossRef]
29. Masoodi Khabar P, Ghydari ME, Vazifeh Shiran N, Shirazy M, Hamidpour M. Platelet MicroRNA-484 as a novel diagnostic biomarker for acute coronary syndrome. *Lab Med*. 2023;54(3):256-261. [CrossRef]
30. Lai N, Wu D, Liang T, et al. Systemic exosomal miR-193b-3p delivery attenuates neuroinflammation in early brain injury after subarachnoid hemorrhage in mice. *J Neuroinflammation*. 2020;17(1):74. [CrossRef]
31. Wong LL, Armugam A, Sepramaniam S, et al. Circulating microRNAs in heart failure with reduced and preserved left ventricular ejection fraction. *Eur J Heart Fail*. 2015;17(4):393-404. [CrossRef]
32. Bai Y, Wang M, Yang Y, Liu X, Chen Q, Guo Z. Inhibition of the miR-193b-3p protects against oxidized low-density lipoprotein-induced HUVECs injury by upregulating ALDH2. *Cell Biol Int*. 2022;46(2):192-202. [CrossRef]
33. Zhang J, Niu J, Tian B, Zhao M. microRNA-193b protects against myocardial ischemia-reperfusion injury in mouse by targeting mastermind-like 1. *J Cell Biochem*. 2019;120(8):14088-14094. [CrossRef]
34. Ding H, Wang Y, Hu L, et al. Combined detection of miR-21-5p, miR-30a-3p, miR-30a-5p, miR-155-5p, miR-216a and miR-217 for screening of early heart failure diseases. *Biosci Rep*. 2020;40(3):BSR20191653. [CrossRef]
35. Neiburga KD, Vilne B, Bauer S, et al. Vascular tissue specific miRNA profiles reveal novel correlations with risk factors in coronary artery disease. *Biomolecules*. 2021;11(11):1683. [CrossRef]
36. Patterson AJ, Song MA, Choe D, Xiao D, Foster G, Zhang L. Early detection of coronary artery disease by micro-RNA analysis in asymptomatic patients stratified by coronary CT angiography. *Diagnostics (Basel)*. 2020;10(11):875. [CrossRef]