Review Article

ERA'S JOURNAL OF MEDICAL RESEARCH VOL.7 NO.2

DOI:10.24041/ejmr2020.36

ROLE OF miRNAs IN CORONARY ARTERY DISEASE: A MINI REVIEW

Seema Singh, Syed Tahseen Raza, Nitin Ranjan Gupta, Janhvi Verma

Department of Physiology

Era's Lucknow Medical College & Hospital, Sarfarazganj Lucknow, U.P., India-226003

Received on : 03-07-2020
Accepted on : 11-09-2020

Address for correspondence

Dr. Seema Singh
Department of Physiology
Era's Lucknow Medical College & Hospital, Lucknow-226003
Email: singh_seema2007@yahoo.com
Contact no: +91-7081019666

ABSTRACT

While coronary artery disease (CAD) has become a major threat worldwide, early diagnosis of CAD, based on timely biomarkers, remains a major unmet clinical challenge. Micro-RNAs (miRNAs) play a pivotal role in development of the cardiovascular system while they are associated with multiple cardiovascular diseases. Several cardiac miRNAs (circulating miRNAs) are observable in circulation and function as biomarkers for CVDs diagnosis and therapy. C-miRNAs display various critical features as biomarkers although their distribution is incredibly stable in circulation; their expression is tissue-/disease-specific and can be easily identified using sequence-specific amplification methods. Such circulating-miRNAs features are useful in designing non-invasive assays to track the development of CVDs. Given substantial success in serum and plasma identification of c-miRNAs. There are several conflicting studies on the alterations of circulating miRNAs concentration in circulation system. Measurements of microRNA (miRNA, miR) in patients with coronary heart disease are impeded by the confounding effects of medication commonly used in cardiovascular patients.

KEYWORDS: Micro RNA, Coronary Artary Disease.

INTRODUCTION

Coronary arteries supply blood to the muscle of the heart and consist of two main arteries: the right and left coronary arteries and their two branches, the circumflex artery and the left anterior artery (1). Normal coronary artery, similar to other arteries, consists of three well defined layers: intima, media, and adventitia. Those three layers are divided by elastin layers. The internal elastic lamina distinguishes the media from intima and adventitia from media (2). Coronary artery disease (CAD) is the worldwide leading cause of cardiovascular death (CVD) (3). By 2020, an estimated 11.1 million patients worldwide will die of this disease (4). Someone is suffering from heart disease every 26 seconds and in the USA someone dies every minute (5). In Europe, 1 in 5 and 1 in 7 women die from CAD and the disease accounts for 16 to 25 percent of all European men's deaths(6).

miRNA

MicroRNAs (miRNAs) are small non-coding RNAs that participate in post-transcriptional modification of coding RNA. Such non-coding small regulatory RNAs are evolutionarily retained and widely distributed across various species (June eta al; 2011). The first micro RNA in was discovered by Lee et al in 1993 in C. *Elegans*, known as LIN-4 (7). miRNAs as a molecular marker play significant role in the clinical diagnosis due to development in molecular biology techniques (8).

Recently, the detection of the role of miRNAs in the pathogenesis of CAD has reignited the lesson to using them as a treatment and a prognostic predictor for cardiovascular disease. It is now recognized that miRNAs are involved in almost all atherogenesis steps, including endothelial disruption and degradation, monocyte invasion and activation, lipoprotein formation, plaque stabilization, CV system remodeling, and platelet and vascular smooth muscle cell activity. miRNAs control gene expression post transcriptionally by degrading and/or blocking messenger RNA targets (9-10). Each miRNA can target multiple mRNAs and regulate ~60% of protein encoding genes in mammals (11). They have diverse functions in regulating several key biological and cellular processes, including cardiovascular differentiation, proliferation and apoptosis (12). Circulating miRNAs have created great interest in recent years and have been investigated as a source of novel biomarkers for many human diseases (13-15). They are recorded in entire blood, mononuclear peripheral blood cells, platelets, plasma, serum, and other body fluids (16). Regarding the miRNAs have been used as a biomarker in ample CAD studies. They find that the determination of the extent of expression of miRNAs in body fluids has a potential function for early detection, treatment, seriousness evaluation

markers and prognostic indicators.

CAD screening involves ground breaking work beginning with the Framingham risk score as a screening instrument, determining risk factors, as well as more complex and extremely reliable approaches such as coronary angiographies. MiRNAs translated and released from platelet, monocyte, and endothelial cells tend to play a significant role at all stages of CAD. Fichtlscherer and colleagues were the first to investigate levels of circulating microRNAs in CAD patients (17).

Expression of miRNA-17, miRNA-92a, miRNA-126, smooth muscle cell enriched miRNA-145 and inflammatory cell enriched miRNA-155 was markedly down-regulated, whereas cardiomyocyte enriched miRNAs; miRNA-208a and miRNA-133 levels were up-regulated in CAD patients. In addition, Wang et al reported that circulating levels of miRNA-31 and miRNA-720 could be useful and promising biomarkers to detect CAD early on (18).

Another miRNA; miRNA-126-5p, appears to play a significant role in atherosclerosis pathways by controlling endothelial cell activity and promoting endothelial regeneration. According to Li et al, CAD patients had significantly lower plasma levels of miRNA-126-5p and these decreases were associated with plaque formation that was detrimental (19). Similarly, the expression of miRNA-206 and miRNA-574-5p was markedly up regulated in patients with CAD compared with control subjects (20). In addition, another miRNA, miRNA-17-92 clusters, has been reported to be involved in apoptosis in endothelial cells caused by TNF-α (21). In addition, downregulation of its expression has been observed in CAD patients, successfully classifying them from the non-CAD group (21).

There are also many other miRNAs proposed as promising biomarkers to differentiate CAD patients from non-CAD patients. According to Sayed and colleagues, miRNA-765, miRNA-149 and miRNA-424 have proven very useful in distinguishing measures against both healthy and dysfunctional CAD patients (22). In addition, Sheik et. al., demonstrated that miRNA-149 and miRNA-765 level assessment in blood plasma were very useful in classifying with stable as well as unstable CAD patients from healthy controls (23). It has been shown, according to Han et. al., that CAD patients have higher plasma levels of miRNA34a, miRNA-21, miRNA-30a and miRNA-106b compared with controls (24). In comparison, the miRNA-135a to miRNA-147 concentration ratio in CAD patients was 19-fold up regulated relative to healthy subjects. In contrast, Zhou et. al., classified CAD from non-CAD patients using miRNA-206 and miRNA- 574-5p plasma expression (25).

CONCLUSION

With all this in view, the detection of stable circulating miRNAs unlocks a new wave of the most successful CVD biomarkers. Study of miRNAs provide high sensitivity and specificity and also have excellent discriminating ability between patients with or without CAD as well as patients with stable CAD or unstable CAD and patients with or without heart failure. In fact, miRNAs have good prognostic beliefs, improved risk stratification and early identification of patients at high risk for cardiovascular events. The next step is therefore to develop a multivariable panel of miRNAs in combination with other traditional biomarkers, to generate the ideal diagnostic and prognostic algorithms for CVD.

CONFLICT OF INTEREST

Authors have no conflict of interest.

REFERENCES

1. Wittlieb Weber CA, Brothers JA. Coronary Artery Anomalies: Current Recognition and Treatment Strategies. Update on Recent Progress. Curr Cardiovasc Risk Rep. 2014;8:395.
2. Waller BF, Orr CM, Slack JD, et al. Anatomy, histology, and pathology of coronary arteries: a review relevant to new interventional and imaging techniques-Part I. Clin Cardiol. 1992;15(6):451-457.
3. Roth GA, Johnson C, Abajobir A, et al. Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015. Journal of the American College of Cardiology. 2017;70(1):1-25.
4. Mathers CD LD. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med. 2006;3:442.
5. Heart Disease and Stroke Statistics-2009 Update. Circulation. 2009;119:e21-e181.
6. McKeown NM, Meigs JB, Liu S, et al. Carbohydrate nutrition, insulin resistance, and the prevalence of the metabolic syndrome in the Framingham Offspring Cohort. Diabetes care. 2004;27(2):538-546.
7. Pasquinelli AE. MicroRNAs and their targets: recognition, regulation and an emerging reciprocal relationship. Nature Reviews Genetics 2012;13: 271-282.
8. Schmitz U, Lai X, Winter F, et al. Cooperative gene regulation by microRNA pairs and their

identification using a computational workflow. Nucl Acids Res. 2014; 25: 31-38.

9. Bajan S, Hutvagner G. Regulation of miRNA Processing and miRNA Mediated Gene Repression in Cancer. Microrna. 2014;3(1):10-17.
10. Landskroner-Eiger S, Moneke I, Sessa WC. miRNAs as Modulators of Angiogenesis. Cold Spring Harb Perspect Med. 2013;3(2):a006643
11. Tai-You Ha. MicroRNAs in Human Diseases: From Cancer to Cardiovascular Disease. Immune Netw. 2011; 11(3):135-154.
12. Galimberti D VC, Fenoglio C, Serpente M, et al. Circulating miRNAs as potential biomarkers in Alzheimer's disease. J Alzheimers Dis. 2014; 42(4):1261-1267.
13. Khoo SK PD, Kang UJ, Resau JH, et al. Plasma-based circulating MicroRNA biomarkers for Parkinson's disease. J Parkinsons Dis. 2012; 2(4):321-331.
14. Jessica A. Weber DHB, Shile Zhang, et al. The MicroRNA Spectrum in 12 Body Fluids. Clinical Chemistry. 2010; 56(11): 1733-1741.
15. Fichtlscherer S, De Rosa S, Fox H, et al. Circulating microRNAs in patients with coronary artery disease. Circ Res. 2010;107: 677e684.
16. Wang HW, Huang TS, Lo HH, et al. Deficiency of the MicroRNA- 31eMicroRNA-720 Pathway in the Plasma and Endothelial Progenitor Cells From Patients With Coronary Artery Disease. Arterioscler Thromb Vasc Biol. 2014; 34: 857-869.
17. Jansen F, Yang X, Proebsting S, et al. MicroRNA expression in circulating microvesicles predicts cardiovascular events in patients with coronary artery disease. J Am Heart Assoc. 2014; 3: e001249.
18. Fichtlscherer S, De Rosa S, Fox H, et al. Circulating microRNAs in patients with coronary artery disease. Circ Res. 2010;107:677e684.
19. Tang Y, Zhang YC, Chen Y, et al. The role of miR-19b in the inhibition of endothelial cell apoptosis and its relationship with coronary artery disease. Sci Rep. 2015; 5: 15132.
20. Sayed AS, Xia K, Li F, et al. The diagnostic value of circulating microRNAs for middle-aged (40-60-year-old) coronary artery disease patients. Clinics. 2015; 70(4): e257-e263.
21. Ali Sheikh MS, Xia K, Li F, et al. Circulating miR-765 and miR-149: Potential Noninvasive Diagnostic Biomarkers for Geriatric Coronary Artery Disease Patients. Biomed Res Int. 2015; 2015: 740301.
22. Han H, Qu G, Han C, et al. MiR-34a, miR-21 and miR-23a as potential biomarkers for coronary artery disease: a pilot microarray study and confirmation in a 32 patient cohort. Exp Mol Med. 2015; 47: e138.
23. Zhou J, Shao G, Chen X, et al. MicroRNA 206 and MicroRNA 574-5p are highly expression in coronary artery disease. Biosci Rep. 2015; 36(1): e00295.
24. Tie J, Daiming F. Big roles of micro RNAs in tumorigenesis and tumor development. Histology and Histopathology. 2011; 26: 1353-1361.
25. Hui AB, Lenarduzzi M. Krushel T, et al. Comprehensive MicroRNA profiling for head and neck squamous cell carcinomas. Clinical Cancer Research. 2010; 16(4): 1129-1139.

How to cite this article : Singh S., Raza S.T., Gupta N.R., Verma J. Role Of miRNAs In Coronary Artery Disease: A Mini Review. Era J. Med. Res. 2020; 7(2): 217-219.