Editorial

MicroRNAs in acute aortic dissection

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Acute thoracic aortic dissection is a medical emergency and missed or delayed diagnosis or treatment is associated with high mortality. Upon presentation, a combination of predisposing factors, symptoms and signs are used to triage patients with appropriate clinical syndrome into low, intermediate and high detection risk (1). Low risk patients do not proceed to diagnostic imaging but may still have the disease. In this group, a sensitive and specific marker would improve diagnosis and subsequent treatment. Furthermore, in known aortic aneurysms, initial medical management to delay progression is the current approach, followed by surgery when diameter exceeds 5.5 cm. Dissection, however, may occur at smaller diameters, implying that biomarkers for risk assessment and therapeutic targeting are clearly needed.

Abdominal aortic aneurysms (AAA) are of atherosclerotic origin whereas ascending thoracic aortic aneurysms (ATAA) are often familial and associated with connective tissue diseases and bicuspid aortic valve (2). Mutations in genes encoding components of the TGF-β signalling cascade and the smooth muscle contractile apparatus have been reported in ATAA; inversely, descending TAA seem to be associated with atherosclerosis and its precipitating factors (3).

The recent advancement in DNA and RNA sequencing techniques have led to the understanding that around 98% of the human genome contains regions of DNA which code for RNA molecules unable to produce proteins and hence termed noncoding RNAs (ncRNAs). In the search of new markers to identify, monitor and treat aortic aneurysms, microRNAs (miRNAs) have emerged as potential candidates. miRNAs are noncoding RNAs, small in size—as opposed to long noncoding RNAs—which are not translated into proteins but inhibit mRNA translation or promote mRNA degradation. They can be detected in tissue or circulating blood and are stable during storage. They are detected with high sensitivity and specificity using microarrays and quantitative real time-polymerase chain reaction (qRT-PCR). miRNA expression is altered in various diseases and its modulation with antisense inhibition may affect the course of the disease. miRNA therapeutics have been investigated in preclinical and phase I and IIa clinical studies in infectious, malignant and vascular diseases (4).

A number of miRNAs are differentially expressed in aortic aneurysms. In thoracic aortic aneurysms the miRNAs mainly studied are: miRNA-29, which downregulates the expression of extracellular proteins (various collagen isoforms, fibrillin-1 and elastin) and its inhibition attenuates aneurysm expansion (5); miRNA-17, which through TIMP-MMP pathway is also associated with matrix degradation (6); miRNA 143/145, which regulate the phenotype and function of vascular smooth muscle cells (VSMC) (7,8); miRNA 181b, which promotes elastin degradation via TIMP expression (9). Decreased miRNA-133 as well as miRNA-29 were associated with increased aortic diameter, possibly through targeting of MMPs (10). In abdominal thoracic aorta multiple miRNAs have been reported; members of the miR-15 (11), miR-21 (12) and miR-26 families (13), which are all involved in VSMC proliferation and apoptosis, are some of them. As the pathogenesis of TAAs and AAAs differ, the roles of miRNAs may also be diverse.

Dong *et al.* (14) now report that miR-15a has significantly

higher expression in 37 acute aortic dissection (AAD) patients compared to their control group, which includes 17 healthy volunteers and 23 patients with non-dissection pathology (11 patients with acute myocardial infarction, 10 patients with chronic aortic aneurysm and 2 patients with pulmonary embolism) (P=0.008); miR-15a has, therefore, 75.7% sensitivity and 82.5% specificity for AAD diagnosis. Furthermore, comparing the same study group—37 AAD patients—with the small group of 14 chest pain (CP) patients of non-dissection etiology, the expression of miR-15a is again higher (P<0.001), with 75.7% sensitivity and 100% specificity. In the same analysis—37 AAD *vs.* 14 CP patients—miR-23a, let-7b and hcmv-miR-US-33-5p have significantly higher plasma expression levels. Previous work from the same group has shown that miR-29a and 29c are under-expressed in thoracic dissection tissue compared to normal wall and this is associated with collagen deposition. The miR-30 family is also downregulated—except miR-30c—and this is important for MAPK pathway (8).

Further studies are needed to investigate the diagnostic and prognostic value of miRNAs as biomarkers in aortic disease, as well as their role as therapeutic targets by using antisense oligonucleotides strategies. MiRNA-15 seems to be a promising candidate and should be further tested. One must, however, keep in mind that there is a long way from cell cultures and whole animal models to humans and in this long way the paper of Dong *et al.* is a significant contribution.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Rogers AM, Hermann LK, Booher AM, et al. Sensitivity of the aortic dissection detection risk score, a novel guideline-based tool for identification of acute aortic dissection at initial presentation: results from the international registry of acute aortic dissection. Circulation 2011;123:2213-8.
2. Isselbacher EM, Lino Cardenas CL, Lindsay ME. Hereditary Influence in Thoracic Aortic Aneurysm and Dissection. Circulation 2016;133:2516-28.
3. Li Y, Maegdefessel L. Non-coding RNA contribution to thoracic and abdominal aortic aneurysm disease development and progression. Front physiol 2017;8:429.
4. Christopher AF, Kaur RP, Kaur G, et al. MicroRNA therapeutics: discovering novel targets and developing specific therapy. Perspect Clin Res 2016;7:68-74.
5. Boon RA, Seeger T, Heydt S, et al. MicroRNA-29 in aortic dilation: implications for aneurysm formation. Circ Res 2011;109:1115-9.
6. Wu J, Song HF, Li SH, et al. Progressive aortic dilatation is regulated by miR-17 associated miRNAs. J Am Coll Cardiol 2016;67:2965-77.
7. Elia L, Quintavalle M, Zhang J, et al. The knockout of miR-143 and -145 alters smooth muscle cell maintenance and vascular homeostasis in mice: correlates with human disease. Cell Death Differ 2009;16:1590-8.
8. Liao M, Zou S, Weng J, et al. A microRNA profile comparison between thoracic aortic dissection and normal thoracic aorta indicates the potential role of microRNAs in contributing to thoracic aortic dissection pathogenesis. J Vasc Surg 2011;53:1341-9.e3.
9. Di Gregoli K, Mohamad Anuar NN, Bianco R, et al. MicroRNA-181b controls atherosclerosis and aneurysms through regulation of TIMP-3 and elastin. Circ Res 2017;120:49-65.
10. Jones JA, Strou RE, O'Quinn EC, et al. Selective MicroRNA suppression in human thoracic aneurysms relationship of miR-29a to aortic size and proteolytic induction. Circ Cardiovasc Genet 2011;4:605-13.
11. Gao P, Si J, Yang B, et al. Upregulation of MicroRNA-15a contributes to pathogenesis of abdominal aortic aneurysm (AAA) by modulating the expression of cyclin-dependent kinase inhibitor 2B (CDKN2B). Med Sci Monit 2017;23:881-8.
12. Maegdefessel L, Azuma J, Toh R, et al. MicroRNA-21 blocks abdominal aortic aneurysm development and nicotine-augmented expansion. Sci Transl Med 2012;4:122ra22.
13. Leeper NJ, Raiesdana A, Kojima Y, et al. MicroRNA-26a is a novel regulator of vascular smooth muscle cell function. J Cell Physiol 2011;226:1035-43.
14. Dong J, Bao J, Feng R, et al. Circulating microRNAs: a novel potential biomarker for diagnosing acute aortic dissection. Sci Rep 2017;7:12784.

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