

Diagnostic implication of circulating microRNAs in acute aortic dissection

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Acute aortic dissection (AAD) is a devastating disease which has a rapid onset, high mortality but a low early diagnosis rate. Untreated aortic dissection has a mortality rate of 1–2% per hour from onset to 30 days (1). Some of the patients died before surgical treatment and even before the diagnosis was clear. In addition, the diagnosis of AAD is difficult because of its rarity and varied presentation. Misdiagnosis is up to 39% (2). In view of these conditions, early accurate diagnosis and prompt treatment are urgently needed for patients to reduce mortality and improve prognosis.

Until now, the diagnosis of AAD is mainly based on imaging due to their relatively higher sensitivity, such as computed tomography angiography (CTA), transesophageal echocardiography (TEE), or magnetic resonance angiography (MRA), and all has their own strengths and weaknesses (3). However, these invasive and costly detection methods are employed only after typical symptoms onset, rely on the doctor's experience and high index of clinical suspicion. So misdiagnosis is likely to occur in silent patients or patients with other cardiovascular disorders that appear to have similar symptoms. Besides, they are usually time-consuming or limited by unavailability at bedside, which leads to the delays in timely diagnosis and treatment. With the addition of radiation and contrast agents are harmful to the body, rapid, easy and convenient biomarker

has become a research hotspot in recent years. Novel biomarkers characterized by high sensitivity and specificity, as well as suitable for early diagnosis, indeed has great potential to improve the early diagnosis of AAD (4).

We have explored the diagnosis value of D-dimer and fibrin degradation products (FDP) for AAD before, and revealed that FDP and D-dimer were outstanding to distinguishing aortic dissection patients and healthy people (5), and more research on details is continuing. Based on our previous study, the research about diagnostic value of AAD using circulating microRNAs was published in recent issue of *Scientific Reports*. We really appreciated that Dr. Eftihia Sbarouni and Akira Sato put forward their insightful comments on our article. As miRNAs are critical regulators of numerous disease process, several circulating miRNAs are also have been proven to be useful biomarkers to monitor the dilation of the aneurysm (6,7). Kin *et al.* have initially selected several miRNA related fibrosis, inflammation, and endothelium and reported that circulating miRNA expression patterns differ between aortic aneurysm patients and healthy controls, suggesting the diagnostic and therapeutic potential of miRNAs in this disease (6). However, there are fewer studies on aortic dissection related to miRNA, and the number of patients is relatively small (8). In our study, we investigated the possibility of plasma microRNAs as biomarkers for AAD diagnosis. As a result,

we found plasma level of miR-15a were significantly higher in the AAD group than in the control group (including healthy controls, acute myocardial infarction, pulmonary thromboembolism, and aortic aneurysm patients). And plasma miR-23a has a high sensitivity and specificity for differentiating AAD from CP groups, while the D-dimer exhibited an excellent sensitivity for the detection of AAD, but had a lower specificity (9). Although our miRNA array analysis detected several miRNAs with significantly changed expression in AAD patients, we did not confirm function. Further experimental studies are needed to analyze and compare associations between well-reported protein markers for AD and miRNAs. The downstream products of miRNA or whether their accumulation may influence protein expression may be the target of our future research. Additionally, we are also going to explore unknown functions of other miRNAs that were expressed in AAA tissue and plasma. So that the new exploration biomarkers could be an effective complement to the diagnosis of AAD.

As recommended in the two comments, more study is needed to understand the role of microRNAs in patients with inflammatory disorders, to explore how the genetic pathways and metabolic pathways link and function, to give a better comprehension of the precise roles of miRNAs in AAD pathophysiology. It is also needed to develop better animal models that more closely reproduce the human pathophysiological features of AAD when necessary (10). In addition, a good and promising biomarker for AD should be high sensitivity, strong specificity, ability to reflect disease course, fast, easy to use, low price, good clinical application prospect and extensive commercial suppliers. We should understand which miRNA is suitable for these requirements. So there is a long way to go.

In summary, early and effective diagnosis method of AAD is imperative, and biomarkers would show the wide application prospect, especially in suspicious AD patients. This study provides a view of miRNAs that plays an important role in the prognosis of AAD, more research will carry out on finding more single or combined miRNA biomarker of AAD and exploring the pathological processes of AAD with miRNA by prospective multi-center studies in the future.

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Footnote

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