The role of circulating microRNAs in the diagnosis of Takotsubo cardiomyopathy

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Dear Editor,

Takotsubo cardiomyopathy (TTC), also known as Stress cardiomyopathy, is a primary cardiomyopathy characterized by reversible ventricular wall motion abnormality.1 Its clinical manifestations are similar to acute myocardial infarction (AMI).2 So, it could be difficult to differentiate TTC from AMI in the early phases.3 The use of cardiac biomarkers in the diagnosis of TTC might be of considerable value. Until now, many scholars have discussed some novel cardiac biomarkers.4,5 These discussed markers, such as B-type natriuretic peptide (BNP), troponin I (Tnl) and creatine kinase MB fraction (CKMB) provide a desirable diagnostic and prognostic value for TTC.4 However, the above related markers also have their limitations and it may take some time to apply them in routine clinical practice.4,5 In view of this, we need to find better biomarkers for use with TTC. MicroRNAs (miRNAs) are a class of high abundance, evolutionarily conserved, non-coding, small single-stranded RNAs that negatively regulate gene expression through binding on the 3' untranslated region (UTR) of target mRNAs.7 Recently, some discovered miRNAs in body fluids seem promising to be utilized as biomarkers to monitor cardiovascular diseases’ initiation and progression.8 It is believed that expression of circulating miRNAs may reflect disease pathology.

Based on the above background, a professor from the Heart Center of Zurich University, Milosz Jaguszewski thought that miRNAs might be used as diagnostic markers for TTC. Milosz Jaguszewski and his colleagues sought to identify circulating miRNAs suitable for the diagnosis of TTC and for distinguishing TTC from AMI.9 Their research included TTC patients (n=36), ST segment elevation myocardial infarction patients (STEMI, n=27) and healthy controls (n=28). After the preliminary selection of miRNAs, eight kinds of miRNAs were considered for further verification by RT-PCR. Researchers eventually found that, compared with healthy controls, miRNA-16 and miRNA-26a were both up-regulated in patients with TTC (both P <0.001). Compared to STEMI patients, miRNA-16, miRNA-26a and let-7f all increased in patients with TTC (respectively P <0.0001, P <0.05 and P <0.05). As in the previous studies, this study also found that cardiac-specific miRNA-1 and miRNA-133a increased notably in STEMI patients compared with healthy controls (both P <0.0001). In addition, miRNA-133a increased more in STEMI patients compared with TTC patients (P <0.05).

A unique signature comprising miRNA-1, miRNA-16, miRNA-26a and miRNA-133a distinguished TTC patients from healthy controls [area under the curve (AUC) 0.835, 95% CI 0.733-0.937, P <0.0001] and STEMI patients (AUC 0.881, 95% CI 0.793-0.968, P <0.0001). In comparison of TTC patients with healthy controls, the sensitivity and specificity of these markers were 74.19% and 78.57%; in comparison TTC patients with STEMI patients, the sensitivity and specificity were 96.77% and 70.37%. The researchers also found that, compared with healthy controls, the plasma endothelin -1 (ET-1) in TTC patients was elevated. However, the ET-1 regulator, miR-125a-5p was reduced in parallel.

In the clinic, diagnostic biomarkers remain an important tool in risk prediction, and determining treatment options during the acute phase of different disease processes. Milosz Jaguszewski and his colleagues have found that four kinds of circulating miRNAs can better distinguish between TTC and STEMI patients. They demonstrate for the first time a unique signature of circulating miRNAs for the sensitive and specific identification of TTC and for distinguishing TTC from STEMI patients. This signature may hold great promise to become an important diagnostic tool for the diagnosis of TTC, just like the discussed markers (BNP and Tnl). The true roles of circulating miRNAs need to be confirmed in a larger patient population in prospective investigations.

Statement of ethical publishing

The authors state that they abide by the statement of ethical publishing of the International Cardiovascular Forum Journal10

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