Short Communication

Interventional Cardiology

Is Takotsubo syndrome a diastolic disorder? New data from AI studies

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About the Study

Takotsubo Syndrome (TTS, also named stress-induced cardiomyopathy or apical ballooning syndrome) is an acute and reversible ventricular dysfunction of the heart, in the absence of obstructive coronary artery disease. Likely due to the rising prevalence of modern life stressors and greater awareness of TTS by medical communities, TTS has been increasingly found worldwide [1-3], including those recently reported from the first Chinese TTS registry (ChiTTS registry) [4]. Although TTS still predominantly occur in elderly women, and is triggered by mental stress, it also happens in men and to be triggered by physical stress (with likely worse outcomes), which has been particularly true during COVID-19 pandemic time [5].

TTS is not to be a benign disorder despite the recovery of its systolic function later. Long-term outcomes of TTS survivors are actually comparable with those of acute myocardial infarction, and all-cause death is more than 5% per year [6]. An essential proportion of TTS patients are left with persistent cardiovascular abnormalities, leading to reduced quality of life and chronic complications including arrhythmias, reduced myocardial reserve, and compromised exercise capacity [7]. Considering relatively low in-hospital mortality rate [4], the onset of TTS has actually become a vital predictor of follow-up problems. Secondary prevention is evidently needed for TTS patients. Nevertheless, poor phenotypic grouping of TTS patients prevents effective therapeutic strategies for long-term risk reduction.

Recently, spatiotemporal Deep Convolution Neural Networks (DCNNs) have been developed to help imaging diagnostic and prognostication of TTS patients [8,9]. The spatiotemporal modeling helped identify cardiac motion patterns through cumulative evaluation of the continuous and multi-dimensional movements of different parts of the myocardium, uncovering a predictive ability that is lost by human interpretation. Of note, when the deep feature visualization and attribution techniques are applied to the proposed DCNN models, latent spatiotemporal features can be identified in association with adverse cardiovascular outcome in TTS patients, so as to recapitulate cardiac structural/functional abnormalities for exploring the pathophysiology of TTS and its outcome correlates. With DCCN temporal arm's saliency visualization on established spatiotemporal DCNNs, a distinctive regional myocardial motion pattern in TTS patients has been found, and confirmed by traditional echocardiography optical flow, speckle tracking and tissue Doppler techniques [10]. These results showed that myocardial stiffness and impaired diastolic mechanics might pre-exist in an essential potion of TTS patients, contributing to their adverse long-term outcomes. Additional information obtained with Cardiac Magnetic Resonance (CMR) and Positron Emission Tomography (PET) may allow a more reliable assessment of the extent of myocardial fibrosis and ventricular stiffness. Down the road, factoring in characteristic imaging features from multi-modality imaging approaches would likely further TTS phenomapping, which gives added impetus to identify homogeneous TTS populations with diastolic dysfunction and develop personalized treatment.

The new information on the prognostic role of diastolic dysfunction in TTS patients have relevant clinical implications. To date there is no specific medication proven to be definitively effective in improving long-term outcome or reducing recurrence of TTS in randomized controlled trials. Evidence is accumulating that the expected benefit of beta-blockers may depend on the precise identification of the patients during the acute phase who are most likely to benefit in a long run [11]. In the study from Italian TTS network, beta-blockade was associated with a lower mortality at long-term follow-up, particularly in hypertensive TTS patients [12], with likely pre-existing myocardial hypertrophy/ stiffness. These results have been recently reiterated by the ChiTTS registry study [4].

Conclusion

Identification of more homogenous TTS patients with diastolic dysfunction and validate the long-term effects of specific treatment strategies would likely become a vital research aim in the future, to evaluate which specific group of TTS patients might benefit from personalized treatments that have been shown to be useful to improve diastolic performance, such as Angiotensin-Converting Enzyme (ACE) inhibitors, Angiotensin II Receptor Blockers (ARBs), calcium channel blockers and mineralocorticoid receptor antagonists, and newly developed ones.

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