中文題目：Dapagliflozin 透過調控內質網壓力改善糖尿病心肌病變

英文題目：Dapagliflozin improves subclinical myocardial function in diabetes through suppressing ER stress: from bedside to bench

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Abstract

Dapagliflozin (DAPA) -- a sodium glucose cotransporter 2 (SGLT2) inhibitor, is currently approved for the treatment of patients with diabetes. DAPA-HF trial disclosed its benefits in symptomatic heart failure, but the mechanism underlying how DAPA mitigates subclinical myocardial dysfunction remains largely unknown.

In this longitudinal and prospective study, we investigated the changes of left ventricular (LV) function including speckle tracking parameters in diabetic patients free from symptomatic heart failure at baseline and six months post DAPA treatment. LV diastolic function and longitudinal strain were also measured sequentially. Using streptozotocin-induce diabetic rat model, we measured the effects of DAPA on myocardial function. In patients with diabetes, following six months of treatment with DAPA, while no significant changes were evident in LV ejection fraction, the diastolic function and longitudinal strain improved. Likewise, in the rat study, compared to control, the diabetic rat heart developed pronounced fibrosis, a decline in strain and overall hemodynamics, all of which were markedly mitigated by DAPA treatment. In contrast, despite insulin exerting a targeted glucose lowering effect, it failed to improve myocardial function and fibrosis. In our in vitro study, under high glucose cardiomyocytes showed significant activations of apoptosis, reactive oxygen species and ER stress associated proteins, which were attenuated by the co-incubation of DAPA. Mechanistically, DAPA, acts by suppressing ER stress, to reduce myocardial fibrosis and improve overall function. The results shown here can lead to further improvement in management of LV diastolic function and strain in diabetic patients with subclinical myocardial dysfunction.

Key words: Dapagliflozin (DAPA); global longitudinal strain (GLS); diastolic function; cardiac fibrosis; ER stress, apoptosis