Dapagliflozin effect on functional mitral regurgitation and myocardial remodeling (DEFORM trial)

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Funding Acknowledgements: None.

Background: Functional mitral regurgitation (FMR) has already been demonstrated to lead to various adverse outcomes. However, the therapeutic effect of current guideline-directed medical therapy (GDMT) in FMR still remained limited. The purpose of this study was to assess the efficacy of sodium-glucose cotransporter 2 (SGLT-2) inhibitor dapagliflozin in reducing the extent of mitral regurgitation and myocardial remodeling in FMR patients.

Methods: In this prospective, randomized, parallel controlled trial, we randomly assigned 104 patients with moderate or severe FMR in a 1:1 ratio to receive either dapagliflozin 10mg once daily or not in addition to GDMT for FMR and follow-up for 12 weeks. The primary outcome was the change in effective regurgitant orifice area (EROA) of mitral regurgitation. Secondary outcomes included changes in regurgitant volume (RV), left atrial dimension (LAD), left ventricular end-systolic dimension (LVESd), left ventricular end-diastolic dimension (LVEDd), left ventricular ejection fraction (LVEF) and E/e' ratio. Furthermore, we additionally compared the occurrence rate of hospitalization for heart failure or cardiac death between groups.

Results: Dapagliflozin was associated with a significant reduction in EROA of FMR (-0.074±0.099 cm² vs. -0.030±0.058 cm² for dapagliflozin vs. control, P=0.008). Dapagliflozin was also associated with significant reduction of RV (-9.08±15.27 ml vs. -2.98±9.28 ml for dapagliflozin vs. control, P=0.017), LAD (-2.45±4.44 mm vs. -0.36±3.08 mm for dapagliflozin vs. control, P=0.007) and E/e' ratio (-5.88±7.41 vs. -1.98±7.63 for dapagliflozin vs. control, P=0.011), and improvement in LVEF (6.57±10.10% vs. 1.92±9.57% for dapagliflozin vs. control, P=0.017). There were no significant differences in the changes of LVESd (P=0.662) and LVEDd (P=0.677) between groups. Hospitalization for heart failure occurred in 6 patients of dapagliflozin group (11.5%) and 10 patients of control group (19.2%) (log-rank test, P=0.257), and 1 patient in dapagliflozin group (1.9%) and 2 patients in control group (3.8%) had cardiac death during the 12-week follow-up (log-rank test, P=0.552).

Conclusion: Dapagliflozin could further reduce the extent of mitral regurgitation and improve myocardial remodeling in FMR patients based on the current GDMT. Our findings suggest that SGLT-2 inhibitors might be considered for GDMT of patients with moderate or severe FMR.