Effect of empagliflozin on CMR-estimated pulmonary capillary wedge pressure in patients with type 2 diabetes, or prediabetes, and heart failure with reduced ejection fraction (SUGAR-DM-HF)

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Background/Introduction: Pulmonary capillary wedge pressure (PCWP) is a measure of left ventricular (LV) filling pressure usually invasively assessed during right heart catheterisation. A cardiac magnetic resonance (CMR) imaging-based model to non-invasively estimate PCWP was recently developed.

Purpose: In this exploratory analysis of the SUGAR-DM-HF trial (NCT03485092) we assessed the association of CMR-estimated PCWP (CMR-PCWP) with other imaging and circulating biomarker measures of congestion in patients with heart failure and reduced ejection fraction (HFrEF) and type 2 diabetes or prediabetes. We also investigated the effect of empagliflozin on CMR-PCWP and the relationship between CMR-PCWP and the remodelling effect of empagliflozin.

Methods: A total of 105 patients with HFrEF were randomly assigned 1:1 to empagliflozin 10 mg once daily or placebo. CMR-PCWP and other ultrasound and circulating biomarker measures of congestion were estimated at baseline and 36 weeks. CMR-PCWP (mmHg) was calculated using the formula: 6.1352 + (0.07204*left atrial volume) + (0.02256*LV mass).

Results: 105 patients with HFrEF, mean age 69 years, 73% males, mean left ventricular ejection (LVEF) 33% were randomised. Mean baseline CMR-PCWP was 15.0 mmHg. CMR-PCWP was ≥15 mmHg in 52 (50% patients) at baseline. At baseline, patients with higher PCWP (≥15 mmHg) were more frequently male, had higher body mass index, higher N-terminal pro-B-type natriuretic peptide (NT-proBNP), and a greater number of B-lines on lung ultrasound (LUS). Peripheral oedema was present in 69% and 57% of patients with higher and lower PCWP, respectively (p = 0.18). Pulmonary crepitations were present in 13% and 11% of patients with higher and lower PCWP, respectively (p = 0.74). At baseline, CMR-derived PCWP correlated with log-NT-proBNP (r = 0.31, p<0.001), left atrial (LA) volume (r = 0.94, p<0.001), E/e’ (r = 0.36, p = 0.02), MRI-derived LV volumes (LV end-systolic volume: r = 0.56 p<0.001; LV end-diastolic volume: r = 0.62 p<0.001), LVEF (r=-0.26 p = 0.01), and right ventricular (RV) volumes (RV end-systolic volume: r = 0.56 p<0.001; RV end-diastolic volume: r = 0.61 p<0.001). Mean CMR-PCWP decreased from baseline to 36 weeks by -0.37 (95% CI -0.78 to 0.05) mmHg and -0.17 (95% CI -0.69 to 0.36) mmHg in the empagliflozin and placebo groups, respectively; placebo-corrected difference -0.43 mmHg (95% CI -1.09 to 0.23), p = 0.20 (Figure 1). The beneficial effect of empagliflozin on reducing LV end-systolic volume index was not modified by baseline CMR-PCWP (p interaction = 0.98).

Conclusions: In patients with HFrEF, higher non-invasively measured CMR-derived PCWP was associated with NT-proBNP, MRI-derived LV and RV volumes and LUS markers of congestion. There were no between group difference in CMR-derived PCWP, although this study was not powered for this outcome.

Figure 1. Change in CMR-derived PCWP between placebo and empagliflozin at 36 weeks follow up.