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LETTER TO THE EDITOR

Effects of sodium-glucose cotransporter 2 inhibitors on pulmonary artery pressure in patients with chronic heart failure

Approximately 50% of patients with chronic heart failure (HF), whether with preserved or reduced left ventricular ejection fraction (LVEF), develop secondary pulmonary hypertension, which is associated with poorer outcomes. Previous studies have shown that sodium-glucose cotransporter 2 inhibitors (SGLT2i) reduce cardiovascular mortality and HF-related hospitalizations in patients with HF, regardless of LVEF.[1,2]

The primary objective of this study is to evaluate the impact of SGLT2i on pulmonary artery pressure (PAP) in patients with chronic HF who are monitored using a PAP sensor (CardioMEMS HF system). A secondary objective is to assess the effects of SGLT2i in patient subgroups stratified by LVEF.[3]

This retrospective study included patients with chronic HF and previously implanted PAP sensors from July 2019 to February 2023. SGLT2 inhibitors were added as a fourth-line treatment in patients with reduced LVEF who were already receiving optimal HF treatment. Patients were excluded if they underwent changes in diuretic therapy or baseline neurohormonal treatment during the follow-up period.

The study compared changes in PAP, renal function, and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels between two time intervals: 1 month before and 1 month after the initiation of SGLT2i therapy. Subsequently, patients were categorized into two groups based on LVEF: group 1 (LVEF $\leq$ 40%) and group 2 (LVEF $>$ 40%), and the same analyses were conducted within each subgroup.

A total of 1020 pulmonary artery pressure (PAP) measurements were analysed from 17 patients included in the study. The mean age was 71.7 ± 9.6 years, with 64.7% being male. The average left ventricular ejection fraction (LVEF) was 49.4 ± 17.5%, 23.5% of patients had an ischaemic aetiology, and 64.7% were classified as New York Heart Association (NYHA) class III. There was a significantly higher proportion of men in group 1 (LVEF $\leq$ 40%) compared to group 2 (LVEF $>$ 40%) (P = 0.043); however, no other baseline characteristics differed significantly between the two groups (*Table 1*). Dapagliflozin (10 mg daily) was initiated in 14 patients (82.4%)—5 in group 1 and 9 in group 2—while empagliflozin (10 mg daily) was initiated in 3 patients (17.6%)—1 in group 1 and 2 in group 2. Prior to the initiation of SGLT2 inhibitor therapy, the mean diastolic PAP (dPAP) was 17.3 ± 5.6 mmHg, and the median NT-proBNP level was 2841.5 pg/mL (interquartile range: 289–10 515 pg/mL).

SGLT2 inhibitors significantly reduced dPAP; the mean dPAP in the "one month after" period was 1.5 mmHg lower (95% CI, 0.26–2.74; P = 0.021) compared to the "one month before" period (*Figure 1*). SGLT2 inhibitors also reduced systolic PAP (−2.2 mmHg), mean PAP (−1.7 mmHg), NT-proBNP (−183 pg/mL), and creatinine (−0.2 mg/dL), although these changes were not statistically significant. These improvements were more pronounced in patients with LVEF $>$ 40% (group 2, n = 11), where a statistically significant reduction in dPAP was observed (−2.04 mmHg; 95% CI, 0.31–3.77; P = 0.025), along with greater declines in NT-proBNP and creatinine.

This real-world study supports and extends the findings of the randomized, double-blind EMBRACE-HF trial,[4] which demonstrated a significant reduction in dPAP in patients treated with empagliflozin alongside standard heart failure therapy. In the EMBRACE-HF study, a reduction in dPAP of up to −1.7 mmHg was observed, which is comparable to the −1.5 mmHg reduction seen in our cohort. The effect on PAP was consistent regardless of systolic function, unlike our results, where the effects were more pronounced in patients with preserved LVEF.

Although the exact mechanism of action remains unclear, several hypotheses have been proposed, including enhanced natriuresis and plasma volume reduction, improved oxygen diffusion, and decreased glomerular pressure.[5,6] Findings from the EMBRACE-HF trial suggest that mechanisms beyond diuresis may play a role in the observed benefits of empagliflozin. Notably, reductions in arterial pressures persisted even 1 week after discontinuation of SGLT2 inhibitors—a sustained effect that cannot be fully attributed to transient diuretic action.

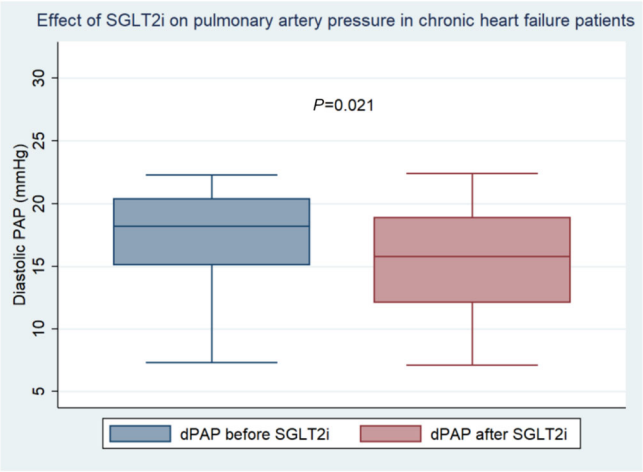
This study is not without limitations. As an observational design comparing patient data before and after treatment, it is inherently susceptible to confounding factors that may influence outcomes.

Table 1 Basal characteristics of chronic heart failure patients, according to left ventricular ejection fraction group

Variables	Total cohort (n = 17)	Group 1 (LVEF ≤ 40%), n = 6	Group 2 (LVEF > 40%), n = 11	P-value
Age, years	71.7 ± 9.6	67.8 ± 10.3	73.7 ± 9.1	0.803
Men, n (%)	11 (64.7)	6 (100)	5 (45.5)	0.043
HT, n (%)	15 (88.2)	6 (100)	9 (81.8)	0.515
DM, n (%)	6 (35.3)	3 (50)	3 (27.3)	0.600
DLP, n (%)	12 (70.6)	4 (66.7)	8 (72.7)	1.000
GFR, mL/min/1.73 m^2	51.7 ± 18.9	51.7 ± 19	51.6 ± 19.9	0.984
Aetiology, n (%)	Ischaemic 4 (23.5) Dilated CM 5 (29.4) HT CM 3 (17.6) HCM 3 (17.6)	Ischaemic 3 (50) Dilated CM 3 (50)	Ischaemic 1 (9.1) Dilated CM 2 (18.2) HT CM 3 (27.3) HCM 3 (27.3) Valvular CM 1 (9.1) TCM 1 (9.1)	0.133
NYHA, n (%)	II 6 (35.3) III 11 (64.7)	II 1 (16.7) III 5 (83.3)	II 5 (45.5) III 6 (54.6)	0.333
AF/Af, n (%)	13 (76.5)	6 (100)	7 (63.6)	0.234
LVEF, %	49.4 ± 17.5	30.7 ± 7	59.6 ± 11.7	0.053
ICD, n (%)	7 (41.2)	4 (66.7)	3 (27.3)	0.600
CRT, n (%)	4 (23.5)	2 (33.3)	2 (18.2)	0.584
Treatments, n (%)	ARNi 5 (29.4) ACEi/ARBs 5 (29.4) BB 13 (76.5) MRA 14 (82.4) HDZ 2 (11.8) Nitrates 4 (23.5) Digoxin 4 (23.5) Diuretics 17 (100)	ARNi 2 (33.3) ACEi/ARBs 2 (33.3) BB 6 (100) MRA 5 (83.3) HDZ 1 (16.7) Nitrates 2 (33.3) Digoxin 2 (33.3) Diuretics 6 (100)	ARNi 3 (27.3) ACEi/ARBs 3 (27.3) BB 7 (63.6) MRA 9 (81.8) HDZ 1 (9.1) Nitrates 2 (18.2) Digoxin 2 (18.2) Diuretics 17 (100)	1.000 1.000 0.237 1.000 1.000 0.584 0.584 0.353

ACEi, angiotensin-converting enzyme inhibitors; AF/Af, atrial fibrillation/atrial flutter; ARBs, angiotensin II receptor blockers; ARNi, angiotensin receptor-neprilysin inhibitor; BB, beta-blockers; CM, cardiomyopathy; CRT, cardiac resynchronization therapy; DLP, dyslipidaemia; DM, diabetes mellitus; GFR-EPI, glomerular filtration rate; HDZ, Hydralazine; HCM, hypertrophic cardiomyopathy; HT, hypertension; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; MRA, aldosterone receptor antagonists; NYHA, New York Heart Association; TCM, tachycardiomyopathy.

Figure 1 Effect of SGLT2i on pulmonary artery pressure in chronic heart failure patients.



In real world ambulatory patients with HF equipped with a PAP sensor, the addition of SGLT2 inhibitors to guideline-directed HF therapy led to a significant reduction in dPAP. While PAP reductions were observed across all patients regardless of LVEF, the effect was more pronounced and statistically significant in those with LVEF > 40%. Further research is warranted to elucidate the underlying mechanisms contributing to these hemodynamic improvements and to assess the long-term durability and clinical implications of these effects.

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References

1. Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, Carson P, Januzzi J, Verma S, Tsutsui H, Brueckmann M, Jamal W, Kimura K, Schnee J, Zeller C, Cotton D, Bocchi E, Böhm M, Choi DJ, Chopra V, Chuquiure E, Giannetti N, Janssens S, Zhang J, Gonzalez Juanatey JR, Kaul S, Brunner-la Rocca HP, Merkely B, Nicholls SJ, Perrone S, Pina I, Ponikowski P, Sattar N, Senni M, Seronde MF, Spinar J, Squire I, Taddei S, Wanner C, Zannad F. EMPEROR-Reduced Trial Investigators. Cardiovascular and renal outcomes with empagliflozin in heart failure. *N Engl J Med* 2020;**383**:1413–1424. doi:10.1056/NEJMoa2022190
2. McMurray JJV, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Martinez FA et al. DAPA-HF Trial Committees and Investigators. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med* 2019;**381**:1995–2008. doi:10.1056/NEJMoa1911303
3. Bayes-Genis A, Pagnesi M, Codina P, Abraham WT, Amir O, de Boer RA, Brugts JJ, Chioncel O, Gustafsson F, Lindenfeld JA, Mullens W, Petrie MC, Rosano G, Metra M. Remote pulmonary artery pressure-guided management of patients with heart failure: A clinical consensus statement of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2025. doi:10.1002/ejhf.3619 Epub ahead of print. PMID: 40288763.
4. Nassif ME, Qintar M, Windsor SL, Jermyn R, Shavelle DM, Tang F, Lamba S, Bhatt K, Brush J, Civitello A, Gordon R, Jonsson O, Lampert B, Pelzel J, Kosiborod MN. Empagliflozin effects on pulmonary artery pressure in patients with heart failure: results from the EMBRACE-HF trial. *Circulation* 2021;**143**(17):1673–1686. doi:10.1161/CIRCULATIONAHA.120.052503
5. Verma S, McMurray JJV. SGLT2 inhibitors and mechanisms of cardiovascular benefit: a state-of-the-art review. *Diabetologia* 2018;**61**:2108–2117. doi:10.1007/s00125-018-4670-7
6. Packer M. SGLT2 inhibitors produce cardiorenal benefits by promoting adaptive cellular reprogramming to induce a state of fasting mimicry: a paradigm shift in understanding their mechanism of action. *Diabetes Care* 2020;**43**:508–511. doi:10.2337/dci19-0074