When should we consider SGLT-2 inhibitors in patients with acute decompensated heart failure?

To the Editor: I read with great interest the excellent narrative review by Badwan et al[1] regarding the use of sodium-glucose cotransporter 2 (SGLT-2) inhibitors in acute heart failure. I thank the authors for their analysis of this complex and exciting topic.

SGLT-2 inhibitors have been shown to be beneficial in the treatment of chronic heart failure as an adjunct to existing guideline-directed medical therapy (angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers/angiotensin-receptor–neprilysin inhibitors plus beta blockade plus mineralocorticoid receptor antagonist with or without device therapy) in several landmark studies. However, I wonder whether the available data have unequivocally shown exactly when and in what sequence SGLT-2 inhibitors should be initiated as adjuncts to loop diuretic therapy in patients with acute decompensated heart failure.

Participants in the DICTATE-AHF (Efficacy and Safety of Dapagliflozin in Acute Heart Failure) trial[2] were prescribed dapagliflozin in addition to protocolized diuretic therapy on day 1 of admission. This trial failed to show a statistically significant change in its primary end point of diuretic efficiency at 5 days compared with placebo, despite augmented natriuresis and 24-hour diuresis.[3] In the DAPA-RESIST (Dapagliflozin Versus Thiazide Diuretic in Patients With Heart Failure and Diuretic Resistance) trial,[4] dapagliflozin was not shown to be more effective than metolazone in improving systemic congestion (note that Badwan et al in Table 1 of their article[1] highlighted a significant weight reduction in DAPA-RESIST participants). In the SOLOIST-WHF (Effect of Sotagliflozin on Cardiovascular Events in Patients With Type 2 Diabetes Post Worsening Heart Failure) trial,[5] patients were prescribed sotagliflozin, a combined SGLT-1/2 inhibitor, after they had already been transitioned from intravenous to oral diuretics, with 51.2% of patients prescribed the drug a median of 2 days after discharge.

As such, I would propose that the best evidence informs the use of SGLT-2 inhibitors after stabilization of acute decompensated heart failure with transition to oral diuretic therapy (with lingering questions about SGLT-1/2 combined vs SGLT-2 therapy). Also, in patients who have not tolerated thiazide-like diuretics due to electrolyte derangements or significant hypotension, SGLT-2 inhibitors may provide a less effective but safer alternative as adjunct sequential nephron-blockade in the acute heart failure setting.

Aditya Sharma, MD, MHPE, FRCPC
Assistant Professor, Department of Internal Medicine, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, Canada

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REFERENCES

1. **Badwan OZ, Braghieri L, Skoza W, Agrawal A, Menon V, Tang WHW.** When should we consider SGLT-2 inhibitors in patients with acute decompensated heart failure? [published correction appears in Cleve Clin J Med 2024; 91(2):118]. Cleve Clin J Med 2024; 91(1):47–51. doi:10.3949/ccjm.91a.23034
2. **Cox ZL, Collins SP, Aaron M, et al.** Efficacy and safety of dapagliflozin in acute heart failure: rationale and design of the DICTATE-AHF trial. Am Heart J 2021; 232:116–124. doi:10.1016/j.ahj.2020.10.071
3. **European Society of Cardiology; Cox ZL.** DICTATE-AHF: efficacy and safety of dapagliflozin in acute heart failure. August 28, 2023. www.acc.org/-/media/Clinical/PDF-Files/Approved-PDFs/2023/03/04/ESC23/28Aug/DICTATE-AHF-esc-2023.pdf Accessed March 15, 2024.
4. **Yeoh SE, Osmanska J, Petrie MC, et al.** Dapagliflozin vs metolazone in heart failure resistant to loop diuretics. Eur Heart J 2023; 44(31):2966–2977. doi:10.1093/eurheartj/ehad341
5. **Bhatt DL, Szarek M, Steg PG, et al.** Sotagliflozin in patients with diabetes and recent worsening heart failure. N Engl J Med 2021; 384(2):117–128. doi:10.1056/NEJMoa2030183