4-2022

Change in Diuretic Dose after Initiation of a SGLT2 Inhibitor in Patients with Heart Failure with Reduced Ejection Fraction

R. Wildemann, PharmD

D. G. Karalis, MD, FACC, FNLA

N. Mirachi, PA-C

B. Thoma, PharmD, BCPS, BCCP

Change in Diuretic Dose after Initiation of a SGLT2 Inhibitor in Patients with Heart Failure with Reduced Ejection Fraction

R. Wildemann, PharmD[1]; D. G. Karalis, MD, FACC, FNLA[2]; N. Mirachi, PA-C[2], B. Thoma, PharmD, BCPS, BCCP[1], R. D'Angelo, PharmD, BCPS[3]

[1]Department of Pharmacy, Thomas Jefferson University Hospital, Philadelphia, PA; [2]Cardiology Consultants of Philadelphia, Philadelphia, PA; [3]Department of Pharmacy, University of Pennsylvania, Philadelphia, PA

Background

- Sodium-glucose cotransporter-2 inhibitors (SGLT2i) are the latest addition to medications that reduce mortality and morbidity in heart failure with reduced ejection fraction (HFrEF)
- Dapagliflozin and empagliflozin are both FDA approved for patients with HFrEF regardless of concomitant type-2 diabetes mellitus
- Multiple mechanisms have been proposed for the cardiovascular benefits of SGLT2i's, including prevention of cardiac remodeling, blood pressure reduction, and improved cardiac energy metabolism
- Inhibition of SGLT2 also causes an osmotic gradient between the glomerular circulation and urinary tubule leading to glucosuria, natriuresis, and diuresis
- The quantity of SGLT2i associated diuresis has not been well defined leading to unclear needs for loop diuretic dose adjustment when initiating a SGLT2i
- The RECEDE-CHF trial showed an approximately 500 mL increase in diuresis over a 24 hour-period after the addition of empagliflozin, but it was limited by a small population (n=23)

Study Purpose

- To identify change in loop diuretic dose when initiating a SGLT2i in patients with HFrEF who are on a stable dose of loop diuretic in the outpatient setting

Methods

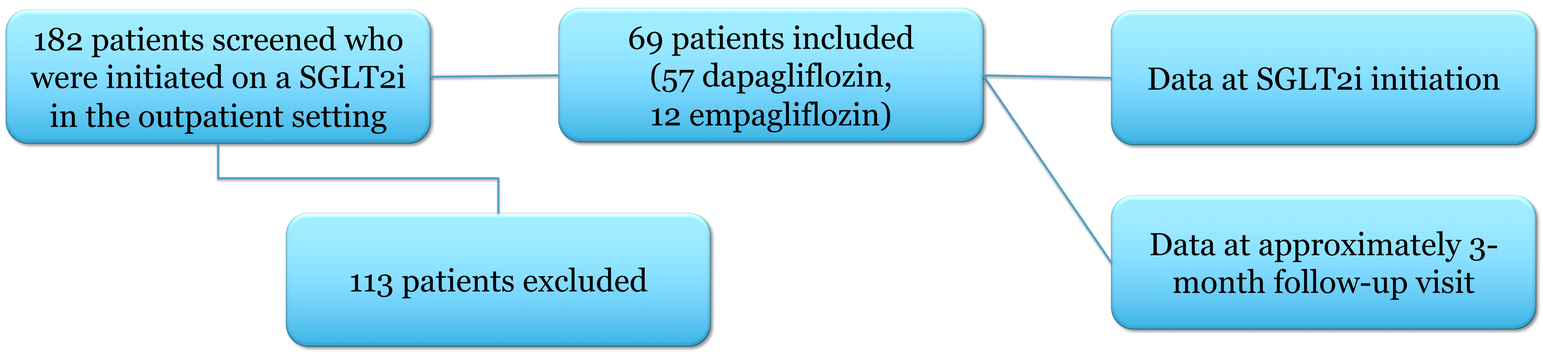
- Retrospective Chart Review
  - 01/01/2020 – 09/30/2021

Inclusion

- Age ≥18 years old
- EF ≤ 40%
- Initiation of SGLT2i as outpatient
- On a loop diuretic prior to SGLT2i initiation

Exclusion

- eGFR <20 mL/min/1.73 m² or dialysis
- SGLT2i discontinued within 3 months of initiation
- Insufficient data in patient's chart or lack of follow-up



Results

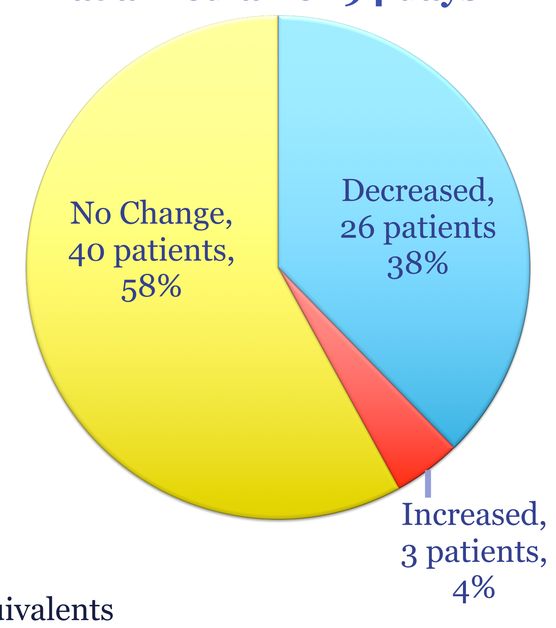
Baseline Characteristics	N = 69
Age in years, median (IQR)	64 (57.5-70.5)
Male	48 (69.6)
Race/Ethnicity	
White	33 (47.8)
African American	30 (43.5)
Other	6 (8.6)
Ejection Fraction, %, median (IQR)	20 (15-30)
NYHA Classification	
I	7 (10.1)
II	29 (42.0)
III	26 (37.7)
IV	2 (2.9)
Unknown	5 (7.2)
Ischemic heart failure etiology	20 (29.0)

All data is n (%) unless noted otherwise.

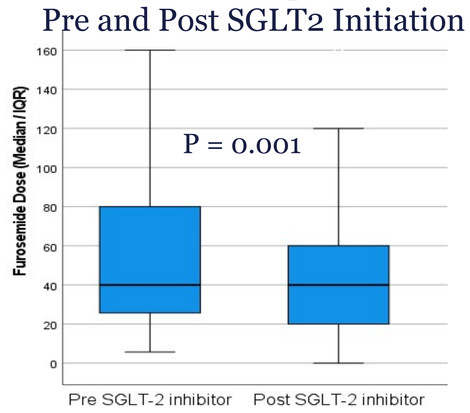
Home medications	N = 69
ACEI/ARB	12 (17.4)
ARNI	51 (73.9)
Beta Blocker	67 (97.1)
Mineralocorticoid Receptor Antagonist	45 (65.2)
Hydralazine/isosorbide dinitrate	4 (5.8)
Digoxin	7 (10.1)
Metolazone	2 (2.9)
Chlorthalidone	0 (0)
Hydrochlorothiazide	0 (0)
Furosemide equivalents, mg, median (IQR)	40.0 (22.9, 80.0)

All data is n (%) unless noted otherwise.

Loop Diuretic Dose Change at a Median of 94 days



Furosemide Equivalents Pre and Post SGLT2 Initiation



No significant differences in secondary outcomes

Outcomes

- **Primary Objective:**

Change in loop diuretic dose at 3 months post-SGLT2i initiation

- **Secondary Objectives:**

Dose change in other diuretic medications, such as thiazide-like diuretics and mineralocorticoid receptor antagonists, at 3 months post-SGLT2i initiation

The patient's HF status based on NYHA classification at 3 months post-SGLT2i initiation

Incidence of adverse effects after SGLT2i initiation (change in serum creatinine, change in serum sodium, and UTI incidence)

Statistical Analysis

Nominal Data	Chi-Squared	N (%)
Continuous Data	Wilcoxon-Signed Rank	Median (IQR)

Conclusions

- While the median loop diuretic dose was similar before and after SGLT2i initiation, there was a statistically significant number of patients who required loop diuretic dose reduction.
- Initiation of a SGLT2i was not associated with a change in NYHA classification or a change in diuretic medications other than loop diuretics
- SGLT2i's were not associated with adverse effects such as change in serum creatinine, change in sodium, change in blood pressure, and urinary tract infections
- When initiating a SGLT2i in a patient with HFrEF, it may be reasonable to consider an empiric loop diuretic dose reduction

Limitations

- Small, retrospective, two-center study
- Only included outpatients initiated on a SGLT2i
- Follow-up limited to approximately 3 months

References

1. Virani SS, Alonso A, Aparicio HJ, et al. Heart Disease and Stroke Statistics-2021 Update: A Report From the American Heart Association. *Circulation*. 2021;143(8):e254-e743.
2. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2013;62(16):e147-e239. doi:10.1016/j.jacc.2013.05.019
3. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *J Am Coll Cardiol*. 2017;70(6):776-803. doi:10.1016/j.jacc.2017.04.025
4. Fathi A, Vickneson K, Singh JS. SGLT2-inhibitors; more than just glycosuria and diuresis. *Heart Fail Rev*. 2021;26(3):623-642. doi:10.1007/s10741-020-10038-w
5. Fitchett D, Inzucchi SE, Cannon CP, et al. Empagliflozin Reduced Mortality and Hospitalization for Heart Failure Across the Spectrum of Cardiovascular Risk in the EMPA-REG OUTCOME Trial. *Circulation*. 2019;139(11):1384-1395. doi:10.1161/CIRCULATIONAHA.118.037778
6. Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med*. 2019;380(4):347-357. doi:10.1056/NEJMoa1812389
7. McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. *N Engl J Med*. 2019;381(21):1995-2008. doi:10.1056/NEJMoa1911303
8. Packer M, Anker SD, Butler J, et al. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. *N Engl J Med*. 2020;383(15):1413-1424. doi:10.1056/NEJMoa2022190
9. Mordi NA, Mordi IR, Singh JS, McCrimmon RJ, Struthers AD, Lang CC. Renal and Cardiovascular Effects of SGLT2 Inhibition in Combination With Loop Diuretics in Patients With Type 2 Diabetes and Chronic Heart Failure: The RECEDE-CHF Trial [published correction appears in *Circulation*. 2020 Nov 3;142(18):e316]. *Circulation*. 2020;142(18):1713-1724. doi:10.1161/CIRCULATIONAHA.120.048739

Disclosure: Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.