Continuation of sodium glucose co-transporter-2 inhibitor therapy in the hospital: Exploring real-world data to understand harms and benefits

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INTRODUCTION

• The anti-hyperglycemic sodium glucose co-transporter-2 inhibitors (SGLT-2i), a class of medications initially made to treat type 2 diabetes mellitus (T2DM), are now approved for heart failure (HF) and chronic kidney disease (CKD) regardless of T2DM status

• SGLT-2i are usually not administered in the hospital setting due to the risk of diabetic ketoacidosis (DKA)

SPECIFIC AIM

• Determine whether continued in hospital use of SGLT-2i is associated with an increased risk of DKA, extended hospital length of stay (LOS), and increased 30-day inpatient readmission rates

HYPOTHESIS

• We hypothesize that continuation of SGLT-2i in the hospital is not associated with increased rates of DKA, increased 30-day inpatient readmission rates, and increased LOS as compared to discontinuation of SGLT-2i in hospital

METHODS

- We accessed TriNetX, a large national database with information on diagnoses and drug exposures for hospital visits, from which we made our cohort
- We indexed the 148,807,502 hospital visits for patients with at least two SGLT-2i prescriptions in 2022 that had an inpatient visit 30 days after the start of at least one of those prescriptions, and kept all visits for each such patient. Of these visits, we then kept only those that were inpatient, with LOS>=2 days, aged >= 18 years old at time of visit, and with at least one SGLT-2i prescription for 30 consecutive days before the visit
- The outcomes of interest for each visit are development of DKA, 30-day inpatient readmission, and LOS
- To account for visit and location clustering, mixed effects models were used
- For 30-day inpatient readmission: mixed effects logistic regression
- For LOS: mixed effects linear model with a log transformation on the LOS

RESULTS

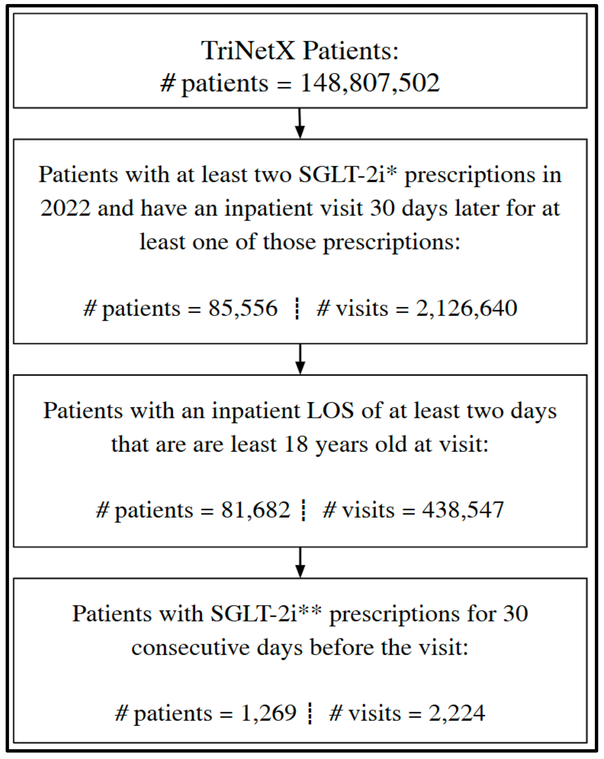

Figure 1. Flowchart of Cohort Selection
*SGLT-2i refers to Canagliflozin, Empagliflozin, or Dapagliflozin
**SGLT-2i refers to Canagliflozin, Empagliflozin, Dapagliflozin, Ertugliflozin, or Bexagliflozin; 2 visits had Ertugliflozin prescriptions prior to admission

Patient Characteristics	N = 2,224[1]
Age at Hospital Visit (years)	64 ± 14
Female Sex	888 (40%)
Race	
White	1,509 (68%)
Black or African American	523 (24%)
Other	165 (7.5%)
Unknown	27 (1.2%)
Ethnicity	
Hispanic or Latino	196 (8.8%)
Not Hispanic or Latino	2,009 (90%)
Unknown	19 (0.9%)
Patient Regional Location	
East North Central	1,129 (51%)
Middle Atlantic	39 (1.8%)
Mountain	1,000 (45%)
West North Central	56 (2.5%)
History of CKD	1,139 (51%)
History of Type 1 Diabetes	93 (4.2%)
History of Type 2 Diabetes	1,739 (78%)
History of Heart Failure	1,646 (74%)
Elixhauser Comorbidity Index	22 ± 17
Used SGLT-2 Inhibitors During Hospital Visit	266 (12%)

[1] n (%); Mean ± SD

Table 1. Patient Characteristics

Clinical Relevant Variables	N = 2,224[1]
30-Day Hospital Readmission	495 (22%)
Development of DKA	12 (0.5%)

[1] n (%); Mean ± SD

Clinical Relevant Variables	N = 2,224[2]
LOS (days)	5.0 (3.0, 8.0)

[2] Median (Q1, Q3)

Table 2. Outcomes of interest

Term	Exp(β)	95% CI for Exp(β)	p-value
Age at visit	0.995	(0.986, 1.004)	0.258
Sex: Male	0.965	(0.769, 1.211)	0.761
Elixhauser score	1.007	(0.999, 1.014)	0.079
History of T1DM	1.065	(0.62, 1.829)	0.82
History of T2DM	1.010	(0.758, 1.345)	0.948
History of HF	0.839	(0.618, 1.137)	0.258
History of CKD	0.996	(0.785, 1.264)	0.977
Prescribed SGLT-2i during visit	1.225	(0.845, 1.775)	0.285

Table 3. Mixed effects logistic regression model for 30-day hospital readmission. Model was adjusted for race and ethnicity. Patient ID and patient regional location are used as random effects.

Term	Exp(β)	95% CI for Exp(β)	p-value
Age at visit	0.996	(0.994, 0.999)	**0.016**
Sex: Male	1.062	(0.988, 1.141)	0.102
Elixhauser score	1.005	(1.002, 1.007)	**<0.001**
History of T1DM	0.998	(0.835, 1.193)	0.982
History of T2DM	0.969	(0.888, 1.058)	0.482
History of HF	1.014	(0.925, 1.112)	0.768
History of CKD	1.053	(0.978, 1.134)	0.174
Prescribed SGLT-2i during visit	1.046	(0.939, 1.165)	0.411

Table 4. Mixed effects linear regression model for LOS. Model was adjusted for race and ethnicity. Patient ID and patient regional location are used as random effects.

DISCUSSION

• SGLT-2i were continued only in 266 visits (12%) during hospitalization

• There were only 12 visits (0.5%) where DKA was documented

• All cases of DKA occurred in patients who were not on SGLT-2i during their hospital stay

CONCLUSIONS

• The number of cases with continued SGLT-2i use in the hospital in this cohort is small and reflects current practice.

• We are unable to determine whether SGLT-2i use in the hospital is associated with increased DKA rates as compared to discontinued as a result of small cohort size and small number of DKA developments.

• We did not find a significant association between readmission rate and in hospital use of SGLT-2i. The confidence interval (0.845, 1.775) is wide likely due to small cohort size

• We did not find a significant association between LOS and in hospital use of SGLT-2i. The confidence interval (0.939,1.165) is wide likely due to small cohort size

NEXT STEPS

• Expand TriNetX cohort beyond one calendar year to increase number of eligible visits.

• Consider less restrictive eligibility criteria, such as in number of prescriptions filled prior to admission.

• Euglycemic DKA and medication-induced ketoacidosis may not be identified with ICD codes for DKA. Using diagnostic laboratory results available in the database may uncover missed cases.

• Further understanding of the cases of DKA observed in this cohort may identify modifiable factors that will decrease the risk of DKA among SGLT-2i users

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