Impact of Hospitalization on Continuation of SGLT2 Inhibitors and GLP-1 Receptor Agonists for Comorbidities in Patients with Type 2 Diabetes

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Abstract

Purpose: In the treatment of type 2 diabetes mellitus (T2DM), select sodium-glucose cotransporter 2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists are recommended based on comorbidities such as chronic kidney disease (CKD), heart failure (HF), and atherosclerotic cardiovascular disease (ASCVD). Because guidelines typically recommend insulin for inpatient treatment of T2DM, there is potential that these therapies may be negatively impacted by hospitalization. This study aimed to assess the effect of hospitalization on outpatient T2DM therapy. *Methods*: In this retrospective study, patients were included if they had a diagnosis of T2DM plus a comorbidity (CKD, HF, ASCVD) for which they were prescribed an SGLT2 inhibitor or GLP-1 receptor agonist and had a recent hospitalization and follow-up appointment at an outpatient clinic. Electronic medical records were reviewed to determine if these therapies were continued during transitions of care. Data was analyzed with basic descriptive statistics. *Results*: Thirty-six patients on SGLT2 inhibitor therapy met inclusion criteria. Four (11%) patients were never restarted on therapy outpatient following hospitalization, three of which did not have an appropriate reason for discontinuation. Twenty-two patients on GLP-1 receptor agonist therapy met inclusion criteria. Four (18%) were never restarted on therapy outpatient following hospitalization, two of which did not have an appropriate reason for discontinuation. *Conclusion*: Five out of 58 patients (8.6%) included in the study experienced an inappropriate discontinuation of therapy throughout the transitions of care process. While most patients had their T2DM medication restarted, this study shows hospitalization can impact guideline-directed outpatient therapy.

Keywords: transitions of care, GLP-1 receptor agonists, SGLT2 inhibitors, type 2 diabetes

Background

While there are many options available for the treatment of type 2 diabetes mellitus (T2DM), the current American Diabetes Association guidelines have specific recommendations for chronic therapy based on a patient's pre-existing comorbidities.[1,2,3] According to these guidelines, specific sodium-glucose cotransporter 2 (SGLT2) inhibitors are preferred treatment options for the treatment of T2DM in individuals with chronic kidney disease (CKD), heart failure (HF), or atherosclerotic cardiovascular disease (ASCVD). Select SGLT2 inhibitors are proven to reduce the risk of major ASCVD events and lower the risk of cardiovascular death, all-cause mortality, and hospitalization for HF in individuals with or without cardiovascular disease.[1] Research shows that use of these agents decreases glucose reabsorption, blood pressure, weight, and albuminuria, while maintaining glomerular filtration rate, contributing to significant improvements in CKD patients.[2] Among the class of SGLT2 inhibitors, canagliflozin, empagliflozin, and dapagliflozin are recommended for use, with indications for specific comorbidities varying slightly according to product labeling.

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Guidelines also recommend glucagon-like peptide-1 (GLP-1) receptor agonists as a treatment option for patients with T2DM and ASCVD due to a reduction in the risk of ASCVD events. Among the class of GLP-1 receptor agonists, liraglutide, dulaglutide, and injectable semaglutide are recommended for this indication. These guideline recommendations are based on evidence that treating individuals with these comorbidities with the specific medications listed provides not only control of T2DM but also a significant improvement in comorbidity outcomes.[1,2,3] During hospitalization, guidelines typically suggest insulin as first-line treatment of patients with T2DM. While SGLT2 inhibitors and GLP-1 receptor agonists may be continued in some individuals, many are switched to insulin therapy while hospitalized. Additionally, there are specific reasons why an SGLT2 inhibitor or GLP-1 receptor agonist may be discontinued during hospitalization, such as in the setting of pancreatitis, gastroparesis, acute kidney injury, surgery, or genitourinary infection, among others. While these medications may not be appropriate during hospitalization, they continue to be recommended for chronic therapy when indicated.

According to guidelines, if the patient's home medications are held while inpatient but are appropriate to restart at discharge, these medications should be ordered 1-2 days prior to discharge.[4] Because of the discrepancy between what is recommended for inpatient management of T2DM and outpatient management, the authors theorize that guideline-directed therapy for CKD, HF, and ASCVD in patients with T2DM

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is often interrupted while a patient is hospitalized and may often not be restarted upon discharge. This lack of continuity of care could lead to adverse clinical outcomes and risk of worsening of comorbidities. This study aimed to assess the effect of hospitalization on the continuation of appropriate outpatient, guideline-directed therapy with SGLT2 inhibitors and GLP-1 receptor agonists in patients with T2DM and CKD, HF, or ASCVD.

Methods

After institutional review board approval of this retrospective study, subjects were identified by a review of electronic medical records from an outpatient clinic and nearby hospital from January 2022 to January 2023. Patients included in this study had a diagnosis of T2DM with a matched comorbidity of ASCVD, CKD, or HF; were prescribed an appropriate guideline-directed SGLT2 inhibitor or GLP-1 receptor agonist based on comorbidity, per product labeling; were hospitalized at an associated community hospital within the reviewed timeline; and attended a follow-up appointment at the outpatient clinic with a provider in primary care or endocrinology within three months following hospitalization. After inclusion criteria were met, electronic medical records from both the outpatient clinic and hospital were reviewed to determine the usage of SGLT2 inhibitor and GLP-1 receptor agonist therapy while inpatient, at discharge, and at the post-hospitalization outpatient clinic visit. If the medication was discontinued at any point, the reasoning was listed. The data was analyzed with basic descriptive to evaluate the continuation of guideline-directed therapy in transitions of care.

SGLT2 Inhibitor Results

Thirty-six of the 950 patients reviewed met inclusion criteria. Baseline characteristics are included in Table 1. Matched comorbidities included ASCVD (30), CKD (23), and HF (18) with 24 patients having multiple indications. Prescribed SGLT2 inhibitors included dapagliflozin (8) and empagliflozin (28). Figure 1 provides a description of SGLT2 inhibitor use throughout the transitions of care. Upon review of hospital charts, five individuals had an SGLT2 inhibitor ordered within 1-2 days of discharge, as recommended per guidelines, while 31 did not. Of these, 12 patients did not have an appropriate reason for withholding SGLT2 inhibitor therapy. The remaining patients had the following reasons for withholding therapy while hospitalized: AKI (7), recent surgery (5), genitourinary infection (3), ketoacidosis (2), active insulin infusion (1), and NPO status (1). Twenty patients were appropriately discharged on an SGLT2 inhibitor, while 16 remained off therapy. Of those not discharged on therapy, 12 had no reason listed for not restarting SGLT2 inhibitor therapy. The remaining patients had the following reasons for withholding therapy: AKI (2), requiring surgery (1), and ketoacidosis (1). At the follow-up clinic visit post-discharge, 12 of 16 patients were appropriately restarted on an SGLT2 inhibitor, while four were not. Of those not restarted at the clinic follow-up visit, one had an active urinary infection, while no appropriate reason was identified for the other three patients to remain off therapy.

GLP-1 Receptor Agonist Results

Twenty-two of the 950 patients reviewed met inclusion criteria. Baseline characteristics are included in Table 2. Prescribed GLP-1 receptor agonists included dulaglutide (14), injectable semaglutide (6), and liraglutide (2). Figure 2 provides a description of GLP-1 receptor agonist use throughout the transitions of care. Upon review of hospital charts, none of the twenty-two patients were found to have orders for dulaglutide, liraglutide, or injectable semaglutide 1-2 days before discharge. Further review of the charts showed that two of the twenty-two patients had appropriate reasons documented for discontinuing therapy during hospitalization, including gastroparesis and irritable bowel syndrome. At discharge, ten of the twenty-two patients were restarted on their medication. At the follow-up clinic visit post-discharge, eight of the twelve patients who were not discharged on GLP-1 receptor agonist therapy were restarted, while four were not. Of these four, one had irritable bowel syndrome, one was switched to an appropriate alternative medication option matched to his comorbidity, and no appropriate reason was identified for the other two patients.

Discussion

It has been hypothesized that hospitalization negatively impacts the continuity of guideline-directed medical therapy for T2DM and associated comorbidities. A previous retrospective study showed that while approximately 60% of the patient population analyzed received outpatient oral medications for T2DM, only 20-25% of the same population received oral medications for T2DM within the 60 days following hospital discharge.[5] While this study did not specifically look at SGLT2 inhibitors and GLP-1 receptor agonists in patients with comorbidities, it did highlight the inpatient changes in therapy that are often continued after discharge. It has also been proven that discontinuity of care between inpatient and outpatient settings has been associated with adverse clinical outcomes. A retrospective case-control study of patient medical records in 2016 and 2017 found that patients who did not receive diabetes transitions of care consults had an increase of Hgb A1c of 0.9%. Those who did receive diabetes transitions of care consults showed a decrease of Hgb A1c of 2.9%. This study also showed a reduction in 30-day all-cause readmissions in patients who received transitions of care consults.[6] Additionally, pharmacist involvement in outpatient transitions of care for recently discharged patients with T2DM has shown benefit in decreasing 30-day hospital readmissions[7] and lowering Hgb A1c.[8]

By the end of our study, 32 out of 36 patients remained on SGLT2 inhibitor therapy. One patient had an appropriate discontinuation of therapy, due to an active urinary infection, while three had no appropriate reason documented for

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discontinuation. At the end of the study, 18 of the 22 patients remained on GLP-1 receptor agonists, while two had appropriate discontinuations and two had no appropriate reason documented for discontinuation of guideline-directed therapy. As a whole, five out of 58 patients (8.6%) included in the study experienced an inappropriate discontinuation of therapy throughout the transitions of care process.

Limitations to this study include the retrospective study design, which brought several challenges such as the inability to intervene or ensure all patients had the same baseline labs collected. Additionally, while the total patient population was large, there were few individuals who met inclusion criteria, leading to a small eligible sample size. Since patients who did not have a clinic follow-up visit after discharge were not included, data on this patient population is missing. These individuals may have had a higher rate of inappropriate discontinuations than what was identified in this study due to the lack of outpatient follow up, since it appears that many inappropriate discontinuations were corrected at the outpatient follow-up visit. Finally, patients may have had appropriate reasons for discontinuation of therapy that were not documented clearly in the chart and not taken into consideration.

Future studies should expand on this information and include an assessment of ways to close the gap that remains for people who should be restarted on therapy but are not. At the hospital and clinic sites included in this study, pharmacists were not routinely involved in discharge planning or outpatient follow-up visits for patients with T2DM. Pharmacists should explore potential opportunities to aid in transitions of care for patients with T2DM, with a focus on ensuring proper therapy selection based on comorbidities. In the hospital setting, pharmacists can make recommendations for ensuring that therapy is initiated or resumed 1-2 days prior to discharge when appropriate. Pharmacists involved in patient discharge can also ensure that patients are being sent home with the most appropriate medication regimen based on comorbidities. Outpatient pharmacists in the clinic setting can work to identify and correct gaps that persist following discharge. These examples highlight potential roles for pharmacists to intervene in order to ensure adherence to guideline recommendations regarding medications for comorbidities in T2DM.

Conclusion

As a whole, the large majority of patients in the study were restarted on SGLT2 inhibitor and GLP-1 receptor agonist therapy following hospitalization, whether at hospital discharge or at the post-discharge clinic follow-up appointment. A small percentage remains who never restarted guideline-directed therapy, and further work should be done on both the inpatient and outpatient sides to ensure that hospitalization does not hinder patient use of SGLT2 inhibitors and GLP-1 receptor agonists to treat comorbidities in T2DM.

Conflicts of Interest: None

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Table 1. Patient Characteristics (SGLT2 Inhibitor Group)

Characteristic	SGLT2 Inhibitor Group (n=36)
Age (mean yrs)	70.6±10.4
Sex	
Male (no.)	22
Female (no.)	14
Weight (mean kg)	95.5±32.6
Height (mean cm)	172±9.3
BMI (mean kg/m^2)	31.8±8.4
Hemoglobin A1c (mean %)[a]	8.1±1.2
Primary Diagnoses for Hospitalization[b]	
Cardiac (no.)	16
Endocrine (no.)	9
GI/Liver (no.)	2
Infection (no.)	10
Neurologic (no.)	1
Orthopedic (no.)	1
Pulmonary (no.)	1
Hospital LOS (mean days)	5.2±4.1
Time to Clinic Follow-up Appointment (mean days)	18.1±18.9
Follow-up Appointment Type	
Primary care (no.)	33
Endocrinology (no.)	3

a. Only 15 patients had a baseline hemoglobin A1c during hospitalization.
b. Four patients had two primary diagnoses.

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Table 2. Patient Characteristics: GLP-1 Receptor Agonist Group

Characteristic	GLP-1 Receptor Agonist Group (n=22)
Age (mean yrs)	63.1±10.3
Sex	
Male (no.)	12
Female (no.)	10
Weight (mean kg)	100.9±26.7
Height (mean cm)	174.5±7.7
BMI (mean kg/m^2)	32.9±7.4
Hemoglobin A1c (mean %)[a]	9.5±2.4
Study Drug Distribution	
Dulaglutide (no.)	14
Liraglutide (no.)	2
Semaglutide (no.)	6
CKD (no.)	13
HF (no.)	11
ASCVD (no.)	22
Primary Diagnoses for Hospitalization[b]	
Cardiac (no.)	11
Endocrine (no.)	3
GI/Liver (no.)	3
Infection (no.)	8
Hospital LOS (mean days)	5.1±3.7
Time to Clinic Follow-up Appointment (mean days)	16.3±18.9
Follow-up Appointment Type	
Primary care (no.)	21
Endocrinology (no.)	1

a. Only nine had a baseline hemoglobin A1c during hospitalization.
b. Three patients had two primary diagnoses.

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Figure 1: SGLT2 Inhibitor Results

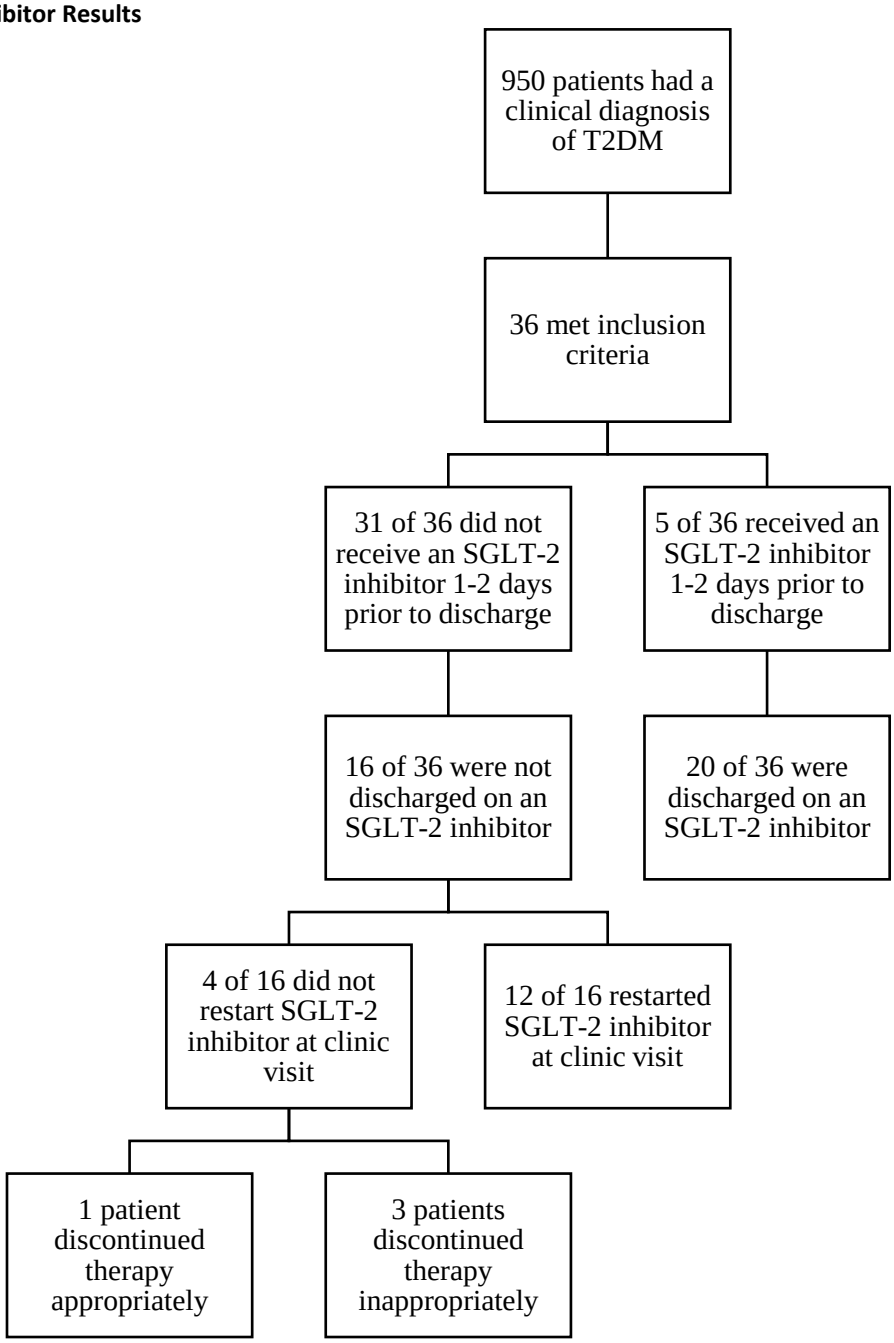

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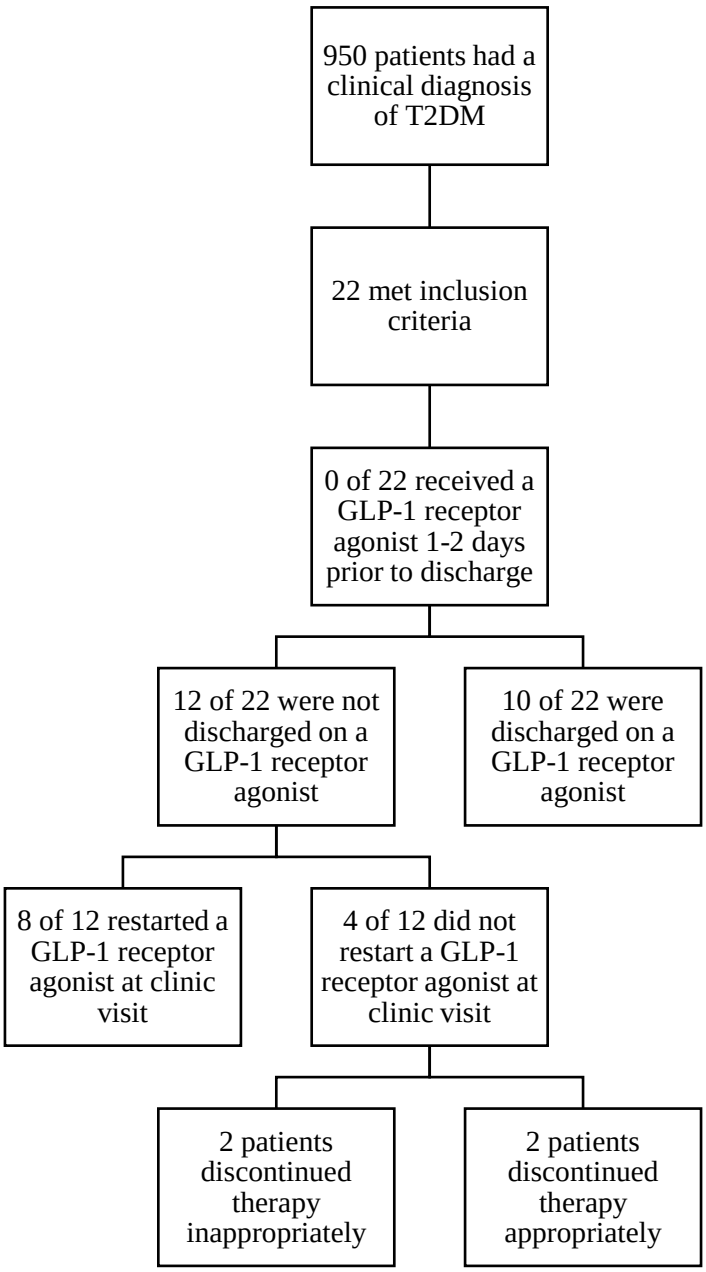
Figure 2: GLP-1 Receptor Agonist Results



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