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Patterns and predictors of antihyperglycemic intensification at hospital discharge for type 2 diabetic patients not on home insulin

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ABSTRACT

Background: Diabetes mellitus is a prevalent condition among hospitalized patients and the inpatient setting presents an opportunity for providers to review and adjust antihyperglycemic medications. We sought to describe practice patterns and predictors of antihyperglycemic intensification (AHI) at hospital discharge for type 2 diabetes mellitus (T2DM) patients not on home insulin.

Methods: We conducted a retrospective study of adult patients with T2DM receiving either non-insulin antihyperglycemic (NIA) or no antihyperglycemic medications prior to admission who were hospitalized within two hospitals in the Johns Hopkins Health System from December 2015 to September 2016. Mean hospital glucose values and observed vs. individualized target hemoglobin A1C values (based on risk of mortality score) were used to define an indication for AHI. Multivariable logistic regression was used to identify predictors of AHI.

Results: A total of 554 discharges of 475 unique patients were included. An indication for AHI was present in 104 (18.8%) of discharges, and AHI occurred in 30 (28.8%) of these discharges. Higher mean admission BG values and A1C, fewer pre-admission antihyperglycemic agents, involvement of the diabetes service, and admitting service were associated with AHI, while no association was observed with age, sex, race, risk of mortality and severity of illness scores, or length of stay. AHI was not associated with 30-day readmission.

Conclusion: An indication for AHI occurs relatively infrequently among hospitalized patients, but when present, AHI occurs in approximately 1 in 3 discharges. AHI appears to be related largely to the degree of hyperglycemia, and diabetes service involvement. Further studies are needed to understand the implications of AHI at hospital discharge on short and long-term outcomes in this population.

Introduction

Diabetes mellitus is a prevalent condition among hospitalized patients affecting ~20% of all hospitalizations in the United States [1]. Although the majority of these patients are hospitalized for reasons other than diabetes [2], the hospital setting presents an opportunity to review and adjust outpatient antihyperglycemic medications not only to avoid short-term complications such as hypoglycemia or severe hyperglycemia, but also to potentially prevent long-term complications in patients who may have limited outpatient follow-up [3–6]. For patients taking non-insulin antihyperglycemic (NIA) medications prior to admission, providers may appraise the appropriateness of continued use of NIA medications at hospital discharge based on observed inpatient glycemic patterns and new comorbidities or contraindications that may arise during hospitalization, while taking into account patient preferences, adherence, and barriers.

When adjusting the outpatient antihyperglycemic regimen at hospital discharge, providers likely rely on clinical practice guidelines targeted to the ambulatory setting [7–9]. The Endocrine Society's inpatient glucose management guidelines suggest reinstitution of the preadmission antihyperglycemic regimen for patients with "acceptable preadmission glycemic control and without a contraindication to their continued use" and "intensification of the outpatient antidiabetic regimen" for those with elevated inpatient glucose [8]. The American Diabetes Association (ADA) recommends consideration of insulin therapy in patients with type 2 diabetes mellitus (T2DM) who have an A1C ≥ 10% and/or blood glucose (BG) ≥ 300 mg/dl, and dual antihyperglycemic therapy for patients with A1C ≥ 9% [9]. For patients with less extreme hyperglycemia, the pharmacological approach depends on the patient's A1C target, which varies amongst clinical

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practice guidelines. The American College of Physicians (ACP) recommends an A1C target of 7–8% for the majority of patients with T2DM, but cautions against targeting specific A1C levels in patients who may be harmed by antihyperglycemic therapy, such as those with limited life expectancy and severe comorbidities [10].

In addition to the ambiguity resulting from different clinical guidelines, medication reconciliation for antihyperglycemic medications at hospital discharge is challenging since the inpatient clinician must consider multiple factors when adjusting medications, including patient's education level and health literacy, timeliness of post-discharge follow-up, and clinical complexity [11–14]. There is currently a lack of clinical decision support to assist inpatient clinicians in individualizing the antihyperglycemic medication regimen at discharge to optimize the benefit to risk ratio for a given patient. Given these challenges, we sought to describe practice patterns of antihyperglycemic reconciliation and to identify factors that influence AHI at hospital discharge for non-insulin treated patients with T2DM. A secondary objective was to explore the association of AHI and 30-day hospital readmissions.

Methods

Study population, setting, and design

This was a retrospective cohort study of adult patients with T2DM receiving either no antihyperglycemic medications or only NIA medications prior to admission who were hospitalized in a non-critical care setting within two hospitals in the Johns Hopkins Health System located in Baltimore, Maryland: Johns Hopkins Hospital (JHH) from July 1, 2016 to September 29, 2016 and Johns Hopkins Bayview Medical Center (JHBMC) from December 1, 2015 to September 29, 2016. During this study period, both hospitals shared the same electronic medical record (EMR) system, EpicCare®.

Hospitalized adults aged < 80 years were eligible for inclusion if a diagnosis of T2DM was present in the EMR (problem list, past medical history, prior admission/discharge diagnoses) at any time prior to the date of discharge or a hemoglobin A1C value ≥6.5% was present in the EMR within 120 days prior to discharge, the patient had an admission length of stay of at least 48 h (to allow providers a sufficient period of observation to determine whether changes were required to the home NIA regimen), and there was at least one BG measurement obtained during hospitalization. Patient admissions with All Patient Refined Diagnosis Related Groups (APR-DRG) Risk of Mortality (ROM) or Severity of Illness (SOI) scores of 4 (extreme) were excluded based on the ACP guidelines, which recommend that "clinicians should … avoid targeting A1C level in patients with a life expectancy less than 10 years due to advanced age (80 years or older)" or with severe comorbidities because the risk–benefit ratio in this population is too high [10]. We also excluded patients on insulin prior to admission because we were interested in understanding factors influencing insulin initiation in this setting, where many patients may already be maximized on NIA therapy with inadequate glycemic control. In addition, we excluded patients who received enteral or parenteral nutrition during hospitalization and women with gestational diabetes and/or delivery within the 30-days prior to hospitalization. This study was approved by the Johns Hopkins School of Medicine Institutional Review Board.

Indication for AHI

Defining indications for AHI at hospital discharge is not straightforward since the hospital-based clinician must consider a broad number of factors when deciding whether to intensify or deprescribe (reduce or stop) medications at the transition from hospital to home. Such factors include personalized glycemic goals, patient preferences, life expectancy, risk of hypoglycemia, and availability and timing of outpatient follow-up [11,13]. Some of these factors cannot easily be collected from the EMR. For the purposes of this study, we defined an indication for AHI based on the patient's risk-adjusted A1C target using the APR-DRG ROM score.

The ROM is a measure of inpatient mortality, which we used in this study as a proxy for longer-term life expectancy to define the patient's individualized A1C target. This is a validated measure that predicts inpatient mortality based on the patient's age, principal and secondary diagnoses, and surgical procedures performed [15–17]. Although individualized glycemic targets may be better guided by consideration of long-term life expectancy in the outpatient setting, we assumed that an inpatient mortality risk measure would more proximally influence antihyperglycemic medication adjustments at hospital discharge. For patients with ROM scores of 1 (minor) or 2 (moderate), we considered the individualized A1C target to be < 8%, consistent with the ACP guidelines that recommend this target for the majority of patients with T2DM. For patients with ROM score of 3 (major), we considered the individualized A1C target to be < 9%. To place these scores in context, studies have shown in-hospital mortality rates for ROM scores of 1, 2, and 3 of 0.5%-2%, 1.7%-5.7%, and 12.3%-17.5%, respectively [18,19].

The admission A1C value was defined as the most recent A1C value occurring within 120 days prior to the date of discharge. Considering that not all hospitalized patients have an A1C obtained during admission and that mean glucose values during admission can provide meaningful information beyond the A1C value, we also used the mean admission glucose value as a secondary criterion for AHI. We converted the A1C cut-offs of 8% and 9% to their corresponding average glucose values of 183 and 212 mg/dl using a published equation [20]. Taking both A1C and mean admission glucose into account, an indication for AHI was deemed to be present if admission A1C was ≥8% or mean glucose was ≥183 mg/dl for patients with ROM-scores of 1 or 2 and b) admission A1C was ≥9% or mean glucose was ≥212 mg/dl for patients with ROM-score of 3; however, since A1C levels and inpatient glucose levels may confer different information about the patient's glycemic control and the need for AHI, we also evaluated AHI in a sensitivity analysis using only A1C criteria (i.e. without imputation of missing results using inpatient glucose levels) to determine indications for AHI (using the same thresholds as above).

Antihyperglycemic intensification patterns

AHI was defined as either NIA intensification, insulin initiation, or both. NIA intensification was defined as an increase in the dose of at least one pre-admission NIA or prescription of at least one new NIA at hospital discharge. Insulin initiation was defined as a prescription for any insulin type at hospital discharge. Deprescribing was defined as a reduction in the total dose or number of NIAs. If NIA was deprescribed but insulin was initiated, AHI was considered to have occurred.

Predictors of antihyperglycemic intensification

We collected data from our EMR and administrative database on variables that might be associated with AHI, including demographics, body mass index (BMI), admitting service, length of hospital stay, SOI score, ROM score, laboratory data, and primary discharge diagnoses. We also collected data on whether a consultation was done by our inpatient diabetes service. Race was categorized as White/Caucasian, Black/African American, or Other. The admitting hospital service was categorized as medical, surgical, intermediate care (IMC) or psychiatry. The primary discharge diagnosis was categorized into major diagnosis categories according to the *International Classification of Diseases* (ICD)-10 codes. Owing to small numbers within individual categories, a diagnosis category of "Other" was created to include: neoplasms, blood diseases, skin diseases, infectious/parasitic diseases, eye/ear diseases, external causes of morbidity and mortality, and factors influencing health status/contact with health services. The SOI and ROM scores are both derived from the APR-DRGs; SOI is a reflection of physiologic

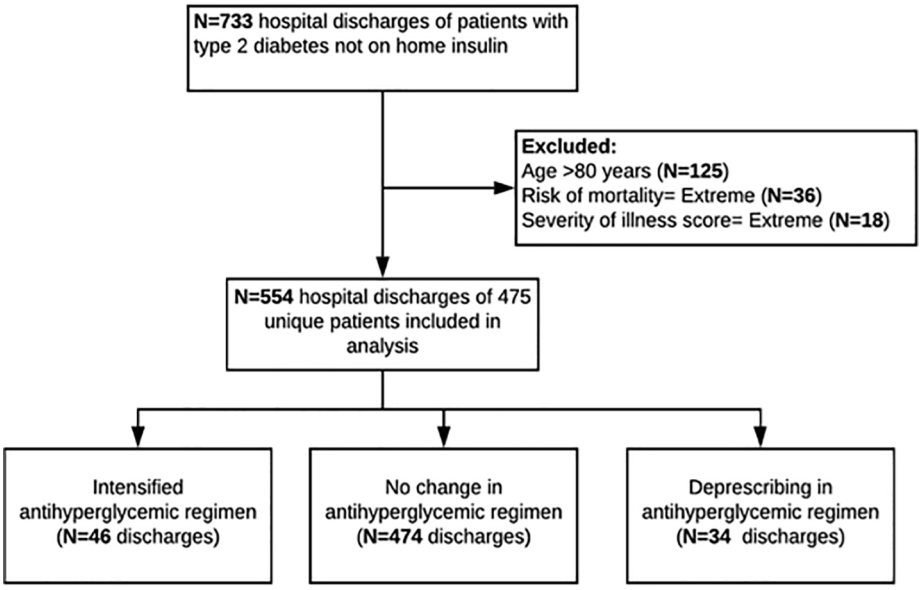

Fig. 1. Study flowchart.

decompensation and is categorized as an ordinal variable of 1 (minor), 2 (moderate), 3 (major) and 4 (extreme), while ROM is a measure of likelihood of inpatient mortality and is similarly categorized as SOI.

Inpatient hypoglycemia was defined as any BG ≤ 70 mg/dl during index admission. A diagnosis of chronic kidney disease (CKD) stage 3–5 was made using either the relevant ICD-10 code from the patient's problem list or past medical history (N18.3, N18.4, or N18.5) or based on the nadir estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) equation during the hospitalization, with stage 1 and 2 CKD combined due to laboratory reporting constraints (i.e. some laboratory results reported as GFR > 60 ml/min/1.73 m^2) [21].

Since the presence of contraindications to one or more classes of NIA agents may influence AHI, we quantified contraindications to the individual NIA drug classes based on a combination of ICD-10 codes, laboratory data, and contraindications specified in the package inserts for individual medications. (Supplemental Table 1).

30-day Readmissions

The secondary outcome was all-cause 30-day readmissions from the date of discharge of the index hospitalization to either of the two hospitals in our health system. Transfers to other inpatient units (e.g. rehabilitation) occurring on the date of discharge of the index admission were not counted as readmissions.

Statistical analysis

Descriptive statistics were used to summarize the patient admission characteristics for the overall population and stratified by AHI status at hospital discharge. For continuous measures, normality of data was assessed using histograms and tests of skewness and kurtosis. Medians and interquartile range (IQR, 25th and 75th percentile) were reported for non-normally distributed variables, and means and standard deviation for normally distributed variables. Number and percentage were reported for categorical variables.

We conducted univariable analyses to compare patient characteristics by the AHI status using Wilcoxon rank-sum test for continuous non-normally distributed variables and Pearson χ^2 test or Fisher exact tests for categorical variables when appropriate. Variables with p-value < 0.2 or deemed to be plausibly related to the outcome of AHI were included in two multivariable logistic regression models. For Model 1, AHI was the dependent variable and age, sex, race, admitting service (medicine, surgery, intermediate care unit, psychiatry), diabetes consult, mean glucose (< 155, 155–212, and > 212 mg/dl), number of pre-admission NIAs (0, 1, 2 or more), ROM score (1, 2, or 3), SOI score (1, 2, or 3), and length of stay. Model 1 included data from the full cohort (N = 554). In Model 2, all the variables above were included with the addition of the admission A1C value. Model 2 included data from 431 discharges in which A1C data was available. To account for multiple admissions during the study period, robust standard error estimates were determined using clustering analysis per unique patient [22,23]. Odds ratios (ORs) were reported with 95% confidence intervals (CI) and two-sided p-value with significance set at 0.05. For the secondary outcome of 30-day readmission, a post-hoc power analysis revealed 80% power to detect an 18% between-group difference in 30-day readmission rate using two-sample proportions test. Statistical analyses were performed using Stata Statistical Software: Release 15 (College Station, TX: StataCorp LP).

Results

The study included 554 discharges of 475 unique patients (Fig. 1). Table 1 shows the characteristics of the study population. Overall, the cohort consisted of an older (median age 62 years), overweight (median BMI 30.2 kg/m^2) population with relatively equal sex and racial (white vs. non-white) distribution. The majority of patients were hospitalized on medical units (60.1%) and had a median (IQR) length of stay of 4 (3–6) days. The study population had fairly good glycemic control on the basis of admission A1C and mean inpatient BG values. A1C results were available for 431 (77.8%) of patient admissions, with a median (IQR) of 6.4% (5.7%-7.1%). The median (IQR) of the mean BG during hospitalization was 132.0 (113.5, 167.4) mg/dl. A diabetes specialist was involved in the care of the patient in 8.5% of discharges.

A contraindication to any NIA was identified in over half of discharges, with over one-quarter having a contraindication to three or more NIA classes. Despite a confirmed diagnosis of diabetes, the majority of patients were not taking any glucose-lowering medications at admission, with nearly one-third taking only one NIA. Very few patients were on two or more NIAs.

Overall, AHI occurred in 46 of 554 (8.3%) discharges, whether or not an indication for AHI was present. Among 104 discharges in which an indication for AHI was present, AHI occurred in 30 (28.8%) discharges. When using only admissions in which A1C values were

Table1
Characteristics of the Study Population Stratified by Antihyperglycemic Medication Reconciliation at Hospital Discharge

Characteristics	Overall	Medication Reconciliation		*P* Value
	N = 554	No change or deprescribing (n = 508)	Intensification (n = 46)	
Age (years), median (IQR)	62.0 (54.0, 71.0)	62.0 (54.0, 71.0)	59.5 (50.0, 70.0)	0.21
Sex: Male, No. (%)	274 (49.5)	248 (48.8)	26 (56.5)	0.32
Race, No (%)				**0.012**
White/Caucasian	281 (50.7)	255 (50.2)	26 (56.5)	
Black/African American	229 (41.3)	217 (42.7)	12 (26.1)	
Other	44 (7.9)	36 (7.1)	8 (17.4)	
BMI (kg/m^2), median (IQR)	30.2 (25.3, 37.8)	30.0 (25.2, 37.8)	30.7 (26.9, 35.3)	0.83
Hospital name, No. (%)				0.58
Hospital 1	393 (70.9)	362 (71.3)	31 (65.4)	
Hospital 2	161 (29.1)	146 (28.7)	15 (32.6)	
Admitting service				< **0.001**
Medicine	333 (60.1)	312 (61.4)	21 (45.7)	
Surgery	104 (18.8)	101 (19.9)	3 (6.5)	
IMC	82 (14.8)	69 (13.6)	13 (28.3)	
Psychiatry	35 (6.3)	26 (5.1)	9 (19.6)	
Length of stay (days), median (IQR)	4.0 (3.0, 6.0)	4.0 (3.0, 6.0)	6.0 (4.0, 8.0)	< **0.001**
Inpatient diabetes consult, No. (%)	47 (8.5)	25 (4.9)	22 (47.8)	< **0.001**
Major diagnostic category, No. (%)				0.093
Circulatory	101 (18.2)	96 (18.9)	5 (10.9)	
Endocrine/metabolic	52 (9.4)	43 (8.5)	9 (19.6)	
Digestive	41 (7.4)	39 (7.7)	2 (4.3)	
Genitourinary	41 (7.4)	39 (7.7)	2 (4.3)	
Mental/behavioral disorders	79 (14.3)	70 (13.8)	9 (19.6)	
Musculoskeletal	33 (6.0)	29 (5.7)	4 (8.7)	
Respiratory	54 (9.7)	49 (9.6)	5 (10.9)	
Nervous system	14 (2.5)	12 (2.4)	2 (4.3)	
Injury, poisoning	29 (5.2)	25 (4.9)	4 (8.7)	
Other	110 (19.9)	106 (20.9)	4 (8.7)	
CKD stage, No. (%)				
Stage 1–2 or none	294 (53.1)	268 (52.8)	26 (56.5)	0.35
stage 3	151 (27.3)	137 (27.0)	14 (30.4)	
stage 4	57 (10.3)	52 (10.2)	5 (10.9)	
stage 5	52 (9.4)	51 (10.0)	1 (2.2)	
Severity of Illness (SOI) score, No. (%)				0.32
Minor	32 (5.8)	28 (5.5)	4 (8.7)	
Moderate	247 (44.6)	231 (45.5)	16 (34.8)	
Major	275 (49.6)	249 (49.0)	26 (56.5)	
Risk of Mortality (ROM) score, No. (%)				0.68
Minor	179 (32.3)	166 (32.7)	13 (28.3)	
Moderate	220 (39.7)	199 (39.2)	21 (45.7)	
Major	155 (28.0)	143 (28.1)	12 (26.1)	
A1C (%), median (IQR)	6.5 (5.8, 7.2)	6.4 (5.8, 7.0)	7.8 (6.9, 11.0)	< **0.001**
Admission A1C*, No. (%)				< **0.001**
< 7%	299 (69.4)	288 (74.4)	11 (25.0)	
7.0%–8.9%	95 (22.0)	80 (20.7)	15 (34.1)	
≥9.0%	37 (8.6)	19 (4.9)	18 (40.9)	
Individualized target A1C				
< 8%	399 (72)	365 (71.9)	34 (73.9)	0.77
< 9%	155 (28)	143 (28.1)	12 (26.1)	
Mean BG (mg/dl), median (IQR)	132.0 (113.5, 167.4)	129.1 (112.3, 158.0)	219.5 (167.6, 270.9)	< **0.001**
Mean admission glucose, mg/dl, No. (%)				< **0.001**
< 155	385 (69.5)	378 (74.4)	7 (15.2)	
155–212	112 (20.2)	97 (19.1)	15 (32.6)	
> 212	57 (10.3)	33 (6.5)	24 (52.2)	
Any BG ≤70 mg/dl	43 (7.8)	41 (8.1)	2 (4.3)	0.56
Change in antihyperglycemic regimen				< **0.001**
Decrease in NIA	34 (6.1)	34 (6.7)	0 (0.0)	
No change	474 (85.6)	474 (93.3)	0 (0.0)	
Increase in NIA	19 (3.4)	0 (0.0)	19 (41.3)	
Decrease in NIA & Addition of insulin	11 (2.0)	0 (0.0)	11 (23.9)	
Addition of insulin	15 (2.7)	0 (0.0)	15 (32.6)	
Increase in NIA & Addition of Insulin	1 (0.2)	0 (0.0)	1 (2.2)	
Contraindication to any NIA, No. (%)	306 (55.2)	280 (55.1)	26 (56.5)	0.85
Contraindication to 3 or more NIAs, No. (%)	145 (26.2)	135 (26.6)	10 (21.7)	0.47
Pre-admission NIAs taken, No. (%)				0.44
0	309 (55.8)	280 (55.1)	29 (63.0)	
1	180 (32.5)	169 (33.3)	11 (23.9)	
2	55 (9.9)	49 (9.6)	6 (13.0)	
≥3	10 (1.8)	10 (2.0)	0 (0.0)	
All-cause 30 day readmissions, No. (%)	65 (11.7)	63 (12.4)	2 (4.3)	0.10

Abbreviations: No., number; IQR, Interquartile range (25th percentile, 75th percentile; BMI, body mass index; IMC, intermediate care; CKD, chronic kidney diseas; BG, blood glucose; AHI = antihyperglycemic intensification, NIA = non-insulin antihyperglycemic.
*A1C results were available for 431 patient admissions

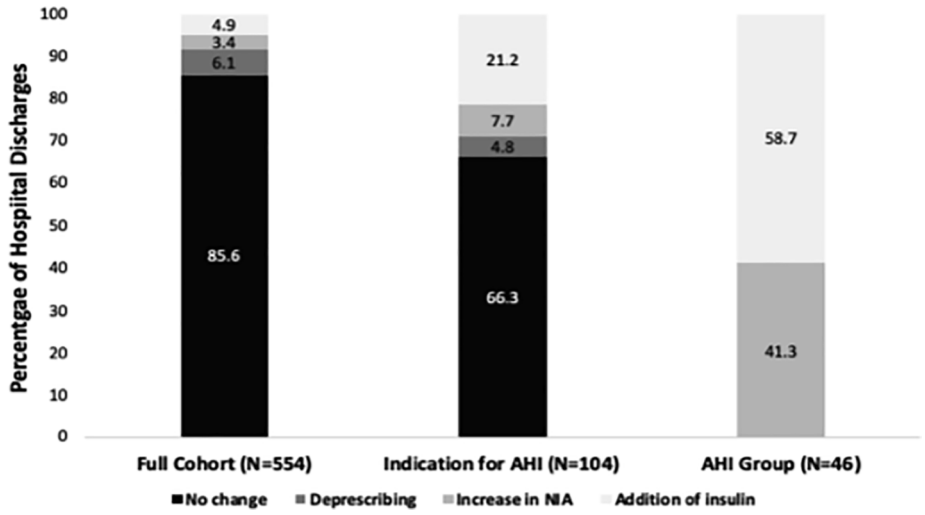

Fig. 2. Patterns of Antihyperglycemic Medication Reconciliation at Hospital Discharge. *Abbreviations*: AHI = antihyperglycemic intensification, NIA = non-insulin antihyperglycemic.

available and only A1C criteria were used to determine indications for AHI (i.e. without imputation of missing results using inpatient mean glucose values), AHI occurred in 21 of 59 (35.6%) discharges."

Fig. 2 shows the patterns of antihyperglycemic medication reconciliation at hospital discharges. Among the full cohort of 554 discharges, 85.6%, 6.1%, 3.4%, and 4.9% had no change in antihyperglycemic regimen, deprescribing of antihyperglycemic regimen, increase in NIA regimen, or addition of insulin, respectively. Among 104 discharges with an indication for AHI, 66.3%, 4.8%, 7.7%, and 21.2% had no change in antihyperglycemic regimen, deprescribing of antihyperglycemic regimen, increase in NIA regimen, or addition of insulin, respectively. Among the 46 discharges in which AHI occurred, 41.3% and 58.7% had an increase in NIA regimen or initiation of insulin, respectively.

There were several notable differences in patient characteristics by AHI status at hospital discharge (Table 1). There was a difference in the racial distribution by AHI status, with slightly more whites, fewer blacks, and more patients from other racial groups in the intensified group compared to the no change/deprescribing group ($P = 0.012$). AHI was higher among patients with admissions to medicine and IMC units, longer length of stay (6.0 vs. 4.0 days; $P < 0.001$), higher admission A1C (7.8% vs. 6.4%, $P < 0.001$), higher admission mean glucose (219.5 vs. 129.1 mg/dl, $P < 0.001$), and for patients seen by a diabetes specialist (47.8% vs. 4.9%, $P < 0.001$). There were no differences in age, sex, BMI, hospital name, admission diagnosis category, CKD stage, SOI or ROM scores, contraindications to NIAs, or number of pre-admission NIAs. We did not observe any significant differences on univariate analysis when using A1C criteria alone (without imputation) to determine indication for AHI.

There was no difference observed in 30-day all-cause readmissions by AHI status, with 63 (12.4%) and 2 (4.3%) being readmitted in the no change/deprescribing and intensification groups respectively (8.1% difference; $P = 0.10$); similarly, among discharges where there was an indication for AHI ($N = 104$), AHI was not associated with 30-day readmissions: 1 (3%) vs. 11 (15%) in the AHI vs. no change/deprescribing groups were readmitted in 30 days (12% difference; $P = 0.095$). It is important to note that this study was powered to detect a minimal between-group difference of 18% with respect to this outcome.

Table 2 shows the predictors of AHI in the univariable and multivariable regression models. On univariable analysis, admission to IMC/psychiatry, mean admission BG, diabetes consult, and admission A1C were all found to be significantly associated with higher odds of AHI. In addition, age and race both had effect sizes with P-values < 0.2, but sex was not significantly associated. In Model 1, which was adjusted for mean glucose and patient admission characteristics, the following variables were predictive of AHI: admission to psychiatry or IMC, mean glucose category, diabetes consult, and number of pre-admission antihyperglycemics. In Model 2, which was additionally adjusted for admission A1C, A1C category was also independently associated with AHI. As expected, in both models, higher glycemic measures were directly associated with AHI in a "dose-dependent" response, with higher odds of AHI occurring with increasing category of glycemic measure (mean BG or A1C). AHI was less likely to occur in patients with two or more pre-admission NIAs. Interestingly, although ROM and SOI would be expected to influence selection of glycemic targets (and, therefore, indication for AHI), we did not observe an association with either measure in relation to AHI after accounting for other confounders.

Discussion

In this study of patients with T2DM treated with NIA medications or no glucose-lowering medications prior to admission, there was a relatively low rate of AHI at hospital discharge. We found an indication for AHI was present in nearly 20% of discharges; however, AHI occurred in only ~29% of these discharges, with insulin initiation occurring in ~21% and increase in NIA in ~8%. At our institution, AHI appears to be driven largely by the level of glycemic control during or prior to admission, the admitting service, involvement of the inpatient diabetes service, and the number of preadmission NIAs being taken. Specifically, AHI is more likely to occur in patients with higher mean admission BGs, higher admission A1C, those taking fewer NIAs, patients admitted to the psychiatry service or IMC, and those seen by our diabetes team.

Not surprisingly, we found that AHI was more likely to occur in those with more severe hyperglycemia. This finding is consistent with a previous study by Griffith et al that showed those who were more likely to have AHI had a higher A1C and higher mean BG on admission [3]. Interestingly, we found that patient already taking two or more NIAs were much less likely to have their antihyperglycemic regimen intensified. Lower rates of NIA intensification or insulin initiation in patients already on NIAs could be related to multiple factors. Inpatient providers may appropriately defer decisions regarding intensification of antihyperglycemic medications to the outpatient setting, where a patient's primary diabetes provider may have a more comprehensive understanding of the patient's diabetes self-management skills and knowledge, social support system, goals of care, and historical response to previous medications.

Additionally, patients who are already on multiple agents may have

Table 2
Univariable and Multivariable Logistic Regression Analysis: Predictors of Antihyperglycemic Intensification at Hospital Discharge

Covariates	Unadjusted ORs		Adjusted ORs			
			Model 1*		Model 2**	
	OR (95% CI)	*P value*	OR (95% CI)	*P value*	OR (95% CI)	*P value*
Age	0.98 (0.95,1.01)	0.13	0.99 (0.96,1.04)	0.972	0.99 (0.95,1.04)	0.913
Sex						
Female	Ref.		Ref.		Ref.	
Male	1.36 (0.74,2.52)	0.32	1.34 (0.58, 3.17)	0.503	1.27 (0.50, 3.25)	0.613
Race						
White/Caucasian	Ref.		Ref.		Ref.	
Black/African American	0.54 (0.27,1.11)	0.09	0.86 (0.33, 2.30)	0.772	0.72 (0.26, 1.98)	0.519
Other	2.18 (0.90,5.25)	0.08	1.49 (0.41, 5.38)	0.541	1.12 (0.27, 4.53)	0.876
Admitting service						
Medicine	Ref.		Ref.		Ref.	
Surgery	0.44 (0.13,1.50)	0.19	0.60 (0.12, 2.90)	0.521	0.66 (0.05, 7.92)	0.747
IMC	2.80 (1.31,5.99)	**0.01**	6.32 (2.06, 19.37)	**0.001**	5.44 (1.71, 17.27)	**0.004**
Psychiatry	5.14 (2.11,12.55)	< **0.001**	5.31 (1.37, 20.59)	**0.016**	4.73 (1.39, 16.05)	**0.013**
Length of stay, days	1.04 (1.01,1.07)	**0.04**	1.01 (0.93, 1.10)	0.865	1.01 (0.93, 1.09)	0.876
Inpatient diabetes consult						
No	Ref.		Ref.		Ref.	
Yes	17.71 (8.75, 35.86)	< **0.001**	14.28 (4.60, 44.40)	< **0.001**	7.17 (2.22, 23.16)	**0.001**
Pre-admission NIAs use						
0	Ref.		Ref.		Ref.	
1	0.63 (0.30,1.30)	0.21	0.21 (0.08, 0.54)	**0.001**	0.13 (0.04, 0.49)	**0.003**
≥2	0.98 (0.38,2.49)	0.97	0.17 (0.05, 0.56)	**0.004**	0.05 (0.01, 0.25)	< **0.001**
Risk of Mortality (ROM)						
Minor	Ref.		Ref.		Ref.	
Moderate	1.35 (0.65,2.78)	0.42	2.13 (0.67, 6.79)	0.199	1.53 (0.49, 4.79)	0.464
Major	1.07 (0.47,2.44)	0.87	2.20 (0.49, 9.84)	0.304	1.80 (0.40, 8.10)	0.439
Severity of Illness (SOI)						
Minor	Ref.		Ref.		Ref.	
Moderate	0.48 (0.15,1.56)	0.23	0.22 (0.03, 1.31)	0.095	0.48 (0.08, 3.01)	0.432
Major	0.73 (0.24,2.27)	0.59	0.20 (0.03, 1.38)	0.102	0.40 (0.05, 3.03)	0.379
Mean admission BG, mg/dl						
< 155	Ref.		Ref.		Ref.	
155–212	8.35 (3.31,21.07)	< **0.001**	9.35 (3.37, 25.97)	< **0.001**	5.99 (2.01, 17.87)	**0.001**
> 212	39.27 (15.65,98.57)	< **0.001**	43.49 (12.96,145.8)	< **0.001**	19.24 (4.48, 82.54)	< **0.001**
Admission A1C, %						
< 7	Ref.		–		Ref.	
7.0–8.9	4.91 (2.15,11.22)	< **0.001**	–		2.73 (0.86, 8.62)	**0.038**
≥9.0	24.80 (10.25,59.99)	< **0.001**	–		10.50 (2.07, 53.32)	**0.005**

*Adjusted for age, sex, race, admitting service, length of stay, pre-admission non-insulin antihyperglycemic (NIA) use, risk of mortality, severity of illness, mean admission blood glucose (BG) (N = 554 discharges).
**Adjusted for all covariates in Model 1 and admission hemoglobin A1C (N = 431 discharges).

fewer available NIAs to select from, as many NIAs are contraindicated based on declining renal function, which is more likely with advancing diabetes disease or duration; however, we did not observe an association between the number of contraindications to NIA drug classes and AHI. Importantly, the development of contraindications to NIAs does not appear to be a significant factor influencing the decision to intensify the antihyperglycemic regimen.

It is important to note that our fully adjusted regression model (Model 2) included only hospitalized patients with diabetes who had a hemoglobin A1C checked during admission (~78% of the entire cohort). As expected, we found a strong positive association between A1C level and likelihood of AHI. When using A1C as an indication criterion for AHI, we found that approximately one-third of eligible admissions had antihyperglycemic treatment intensification at discharge. A1C provides useful information about the quality of outpatient glycemic control and can guide hospital-based clinicians in determining whether hyperglycemia observed in the inpatient setting justifies intensification of the outpatient antihyperglycemic regimen. Thus, in accordance with the ADA standards of care for diabetes care in the hospital, hospital-based clinicians should be encouraged to obtain A1C values for admitted patients with diabetes or hyperglycemia who do not have a result available within the previous 90 days [7].

In our study, involvement of our inpatient diabetes team was strongly associated with AHI. Our diabetes team is not only involved in day-to-day glucose management, but also provides discharge recommendations to the primary team with respect to the anti-hyperglycemic regimen. While inpatient diabetes services have been shown to improve the quality of inpatient glycemic control and other process and outcome measures [24–26], there is less evidence about whether inpatient diabetes consultative care is associated with greater odds of AHI at discharge. Griffith et al found that involvement of the endocrinology team for inpatient glucose management was associated with an adjusted odds of AHI of 4.27 (95% CI, 2.78–6.56) in their cohort of 2025 admission [3]. Although our study had a smaller sample size and adjusted for different factors, we found an even higher odds of AHI among admissions where the diabetes service was involved. The reason for higher rates of AHI on the psychiatry service at our institution is not readily apparent; although patients on psychiatry are more often seen by our diabetes team, the association with AHI persisted after adjustment for diabetes consult.

An unexpected finding in this study was the lack of association between age and AHI. Considering that advancing age may be associated with greater risks of harm from hypoglycemia and/or perceived reduced overall benefit of glycemic control in relation to diminishing life expectancy [10], we expected to find an inverse association between age and AHI. In this study, we excluded patients with age > 80 years and determined individualized glycemic targets based on ROM scores, which takes into account the patient's age and hospital

diagnoses to determine risk of inpatient mortality. Despite the fact that age is factored into the ROM score, it is possible that use of this inpatient mortality measure may not appropriately translate to longer-term mortality (i.e. 5–10 year horizon), which may be more germane to the decision to intensify antihyperglycemic therapy. Additionally, it is possible that the lack of association between age and AHI may be explained by overly liberal glycemic targets in this study, in which 28% of patients had a target A1C < 9%. We recognize that our approach for individualizing glycemic targets may be overly simplistic considering that many other factors (including patient preferences, patient adherence, barriers to self-care, etc.) must be considered when making a decision whether to intensify antihyperglycemic therapy.

We did not find an association between AHI, whether indicated or not, and 30-day readmission in this study; however, our study was not adequately powered to detect this outcome. A retrospective study of nearly 2,000 patients with T2DM found that AHI at discharge was not associated with 30-day readmission overall, but was linked to reduced 30-day readmission and emergency department (ED) visits among patients with elevated A1C levels on medical services [27]. Notably, their cohort included patients taking insulin in the outpatient setting. A very large study by Eby et al found that AHI was associated with higher odds of 30-day readmission in their cohort of 52,000 patients with T2DM [28]. Unlike our study, their cohort included patients on home insulin. Another recent large cohort study of older adults found that insulin initiation at hospital discharge was associated with a higher risk of death, emergency department visits, and readmissions [29].

There were several strengths of this study. Manual chart review was used in combination with extraction of EMR-data to ensure that the exposure variable of interest, AHI, was accurately captured. Importantly, we excluded patients with advanced age and extreme mortality risk in whom the benefits of AHI may be questionable. We carefully assessed the presence of contraindications to NIA drug classes, which may be a factor that influences the ability to intensify therapy in higher risk hospitalized patients. We included a broad number of clinically relevant confounders, but recognize that residual confounding may still be present. This study is limited by the low overall rate of AHI, which limited our power to detect associations of AHI and 30-day readmissions. Furthermore, we restricted our study to non-insulin treated patients with T2DM, which may limit the generalizability of our findings. A1C data were missing from 22.9% of hospitalizations which could introduce an ascertainment bias; however, to overcome this limitation, we included both A1C and inpatient glucose data (which is readily available on all patients) in our definitions for indication for AHI. Finally, hospitalizations occurring outside our medical system and medication compliance could not be captured in this analysis.

In conclusion, clinical inertia regarding antihyperglycemic medications is highly prevalent at hospital discharge, but it is difficult to determine whether this is intentional or unintentional, as inpatient prescribers may perceive reduced benefit relative to risk of adjusting antihyperglycemic medications at this transition of care. We identified inpatient glycemic measures, number of pre-admission NIAs, diabetes service involvement, and admitting service to be the major predictors of AHI. Further qualitative studies of hospital-based clinicians are needed to understand what factors influence their decision to intensify therapy in this population. Prospective studies that randomly assign patients at hospital discharge to different AHI algorithms could evaluate effectiveness on readmissions, quality of outpatient glycemic control, and healthcare expenditures.

Disclosures

The authors have no conflicts of interest to disclose.

Credit authorship contribution statement

Mohammed S. Abusamaan: Formal analysis, Investigation, Project administration, Validation, Writing- original draft, Writing - review & editing. **Betiel Fesseha Voss:** Data curation, Writing - review & editing. **Han Na Kim:** Conceptualization, Data curation, Formal analysis, Investigation, methodology, project administration, writing- review/editing. **Dalilah Reyes-DeJesus:** Data curation, investigation, Writing - review & editing. **Susan Langan:** Formal analysis. **Timothy M. Niessen:** Writing- original draft, Writing - review & editing. **Nestoras N. Mathioudakis:** Conceptualization, Data curation, Formal analysis, Investigation, Supervision, Writing- original draft, Writing - review & editing.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcte.2020.100220.

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