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Intensification of diabetes medication and risk for 30-day readmission

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Abstract

Aim—To examine the association of in-hospital diabetes regimen intensification with subsequent 30-day risk for unplanned readmission/emergency department admission.

Methods—We retrospectively studied 1949 adults with Type 2 diabetes receiving primary care within an academic health network admitted to the hospital between January 2007 and December 2009. Glucose therapy intensification was defined as new start of insulin or oral hypoglycaemic agents, or addition of prandial insulin or insulin mixtures. The association of glucose therapy intensification with subsequent 30-day risk for unplanned readmission/emergency department admission was examined, with focus on medicine service patients with poorly controlled glycaemia (baseline HbA_{1c} ≥ 64 mmol/mol).

Results—One in six patients (324/1949, 17%) had early readmission/emergency department admission. Compared with patients without early readmission, readmitted patients were more often male (58 vs. 52%, $P = 0.03$), had higher Charlson co-morbidity score [mean (SD) 3.0 (2.0) vs. 2.8 (1.8), $P = 0.02$], longer length of stay [5 (4.4) vs. 3.9 (3.3) days, $P < 0.01$] and were more often discharged home with nursing services (38 vs. 32%, $P = 0.03$). Overall, glucose therapy intensification was not associated with early hospital readmission/emergency department admission (odds ratio 0.94, 95% CI 0.64–1.37, $P = 0.74$). However, among medicine service patients with baseline HbA_{1c} ≥ 64 mmol/mol (8%), glucose therapy intensification was associated with a significantly decreased early readmission risk (adjusted odds ratio 0.33, 95% CI 0.12–0.88, $P = 0.03$) and lower post-discharge HbA_{1c} {mean decrease (SD): 20 (26) mmol/mol [1.8 (2.4) %] vs. 7 (15) mmol/mol [0.6 (1.4) %], $P < 0.01$ }.

Conclusions—Diabetes medical regimen intensification during hospitalization was not associated with early readmission. Among patients with elevated HbA_{1c}, glucose therapy intensification was associated with a decreased 30-day readmission/emergency department admission risk and lower outpatient HbA_{1c} levels. Our findings support the safety and durable impact of diabetes regimen optimization during hospital admission.

Introduction

Up to one quarter of hospitalized patients have Type 2 diabetes [1,2] and rates of hospitalization in this group are three times higher than in the general population [3]. Hospitalization has been proposed as a ‘teachable moment’ for chronic conditions during

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Competing interests

None declared.

which patients have intensive contact with a full range of expert clinicians [4,5]. In this paradigm, the time in the hospital, regardless of the reason for admission, represents an opportunity to address diabetes care goals traditionally considered the domain of outpatient management. Although benefits of glycaemic control during hospitalization have been well studied [6–9], there has been limited study of the impact of in-hospital medication changes on subsequent post-discharge outcomes.

Statin initiation is one widely cited example of how hospitalization can lead to beneficial long-term changes in outpatient management [10]. In contrast to statins, however, the medications used to achieve glycaemic control, especially insulin, are more likely to cause adverse events [11,12], raising concern that therapy changes by the hospital care team might result in drug-related complications after discharge [13]. Unplanned early readmissions are a marker for poor healthcare quality [14–16] and early readmission rates in some diabetes patient populations are as high as 20% [17]. Recent studies have shown an association of increased risk for emergency hospitalizations with both outpatient use of insulin and oral hypoglycaemic agents and unintentional discontinuation of chronic care medications in the transition from hospital to home [12,18]. Together, these findings raise questions about the effect of diabetes medication changes during hospitalization on post-discharge outcomes.

We tested the hypothesis that intensification of diabetes medication regimens during hospitalization increased risk of an early hospital readmission or emergency department admission post-discharge.

Patients and methods

Patients and setting

The study was conducted at Massachusetts General Hospital, a 1000-bed tertiary care academic medical centre with 13 affiliated primary care clinics in Boston, Massachusetts. Using a previously described prospective diabetes cohort receiving continuous primary care within the academic health network served by the hospital [19], we identified patients with Type 2 diabetes admitted to Massachusetts General Hospital between 1 January 2007 and 31 December 2009 with no prior admission in 2006. We excluded all patients with index admission to paediatrics, obstetrics and psychiatry services, missing pre-admission or discharge medication data, death during hospitalization and discharge to a facility other than home. Additional pre-specified analyses were performed on a sub-cohort of patients admitted to the medicine service with baseline HbA_{1c} ≥ 64 mmol/mol (8%). There were no ongoing standardized diabetes management or education programmes at the hospital during the study period.

Clinical variables and outcomes

The primary outcome was unplanned hospital readmission or emergency department admission to Massachusetts General Hospital within 30 days of index hospitalization discharge. Planned readmissions were excluded. All HbA_{1c} data were obtained from the hospital laboratory records; all measurements were performed with a high-performance liquid chromatography (HPLC) method that is Diabetes Control and Complications Trial-aligned and serves as one of the primary reference methods for the National Glycohemoglobin Standardization Program [20]. The assay has intra- and interassay coefficients of variation at low and high values that are less than 2%. Baseline HbA_{1c} was defined as most recent HbA_{1c} within 1 year of index hospital discharge date. Baseline HbA_{1c} was not available for 19 patients and was > 1 year from index discharge date in 46 additional patients. Follow-up HbA_{1c} was defined as most recent HbA_{1c} within 1 year after index hospital discharge date.

All inpatient medications from admission through discharge are ordered through our hospital's electronic order entry system. Active outpatient medications at the time of admission were entered electronically into the computerized order entry system by physicians and verified with the patients by their nurses. We assessed in-hospital regimen changes by comparing the pre-admission medication lists with the discharge medication lists obtained via the electronic order entry database. We created the following medication categories for this study: diabetes-related medications (insulin, oral hypoglycaemic agents), anti-hypertensive medications, cholesterol-lowering medications, and oral glucocorticoids.

Changes in diabetes medications were categorized as intensification, de-intensification or no significant change in regimens. Glucose therapy intensification was defined as new start of any class of insulin (short-acting, intermediate-acting, long-acting or insulin mixture) or oral hypoglycaemic agents (biguanide, sulphonylurea, thiazolidinediones, others), or intensification of pre-admission insulin regimens by the addition of prandial (short-acting) insulin or insulin mixtures. Glucose therapy de-intensification was defined as discontinuation of oral hypoglycaemic agents without either starting insulin or another oral hypoglycaemic agent, or discontinuation of long-acting, intermediate-acting and/or short-acting insulin and not starting an insulin mixture. If neither glucose therapy intensification nor de-intensification occurred, the diabetes regimens were considered to have no significant change. Dose changes were not captured in this analysis. Intensification of anti-hypertensive medication regimen was defined as an increase in the number of anti-hypertensive class agents (angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, beta-blockers, alpha-blockers, diuretics, anti-aldosterone, calcium channel blockers and vasodilators); de-intensification was defined as a decrease in the number of anti-hypertensive class agents.

Age, gender, race (white/non-white), primary admission diagnosis, length of stay, admitting service and discharge disposition (home, home with visiting nurse services) were obtained from electronic medical and billing records. Charlson co-morbidity score was determined from administrative coding data from the year of index admission [21]. Scheduled follow-up appointments with primary care physicians and actual follow-up appointments were obtained from electronic scheduling records and confirmed with electronic billing data. High 'primary care physician connectedness', a description of the closeness of the relationship between a patient and their primary care physician, was determined by a previously validated algorithm [22].

Diabetes was considered the primary cause of admission if the primary discharge diagnosis was listed as diabetes [International Classification of Disease (ICD)-9 codes 249.x, 250.x and 251.x]. Hypoglycaemia was considered a reason for hospital or emergency department admission if it was listed as one of the discharge diagnoses or primary complaint on the emergency department discharge summary. Data regarding duration of diabetes and endocrine consultation were not available; however, fewer than 7% of adult inpatients with diabetes received an endocrine consult for diabetes at our institution during the time period of this study.

Statistical analysis

For the primary analysis, we compared baseline unadjusted characteristics using *t*-tests for continuous variables, Fisher tests for dichotomous variables and χ^2 -tests for categorical variables. A pre-specified analysis of the sub-cohort of patients on the medicine service with baseline HbA_{1c} ≥ 64 mmol/mol (8%) compared baseline unadjusted characteristics using *t*-tests or analysis of variance (ANOVA) for continuous variables and χ^2 -tests for categorical variables. Multivariate logistic regression was used to model the primary outcome of readmission or emergency department visit within 30 days of discharge, with intensification

of diabetes medication regimens as the independent variable and age, length of stay, discharge home with visiting nurse services, high 'primary care physician connectedness', Charlson co-morbidity score and baseline HbA_{1c} as covariates. Each patient could only contribute one index hospitalization to the analysis. Covariates were selected based on univariate *P*-values of < 0.1 when comparing patients with and without 30-day primary outcome and between diabetes medication intensification and no intensification groups. All analyses were performed with SAS version 9.3 (SAS Institute, Cary, NC, USA). The protocol was approved by the Partners Healthcare Institutional Review Board.

Results

Patient characteristics, changes in medication regimen and readmission rates

We identified 2631 patients with Type 2 diabetes with admission to Massachusetts General Hospital during the study period. Seventy-eight patients with index admission to paediatrics, obstetrics or psychiatry services, 172 patients with missing pre-admission or discharge medication data and 432 patients who died during hospitalization or were discharged to a facility other than home were excluded, leaving 1949 patients for analysis. Patients had a mean (SD) age of 65 (13) years and mean length of index hospital admission of 4.1 (3.5) days. Baseline HbA_{1c} was available for 1884 (97% of the patients) with average baseline HbA_{1c} of 60 (19) mmol/mol [7.6 (1.8) %], 65 (71) days prior to index discharge. Most patients (91%) had a diagnosis of diabetes documented on admission, of whom 117 (6%) had diabetes listed as the primary reason for admission. The majority of patients (85%) were on diabetes medication at the time of admission; 35% were on insulin.

Three hundred and twenty-four patients (17%) had unplanned readmission or emergency department admission within 30 days of discharge. Patients with early readmission or emergency department admission were more often male (58 vs. 52%, *P* = 0.03), had higher Charlson co-morbidity score [mean score (SD), 3.0 (2.0) vs. 2.8 (1.8), *P* = 0.02], longer length of stay [mean (SD), 5 (4.4) vs. 3.9 (3.3) days, *P* < 0.01], less likely to have high 'primary care physician connectedness' (76 vs. 81%, *P* = 0.04) and were more likely to be discharged home with visiting nurse services (38 vs. 32%, *P* = 0.03) compared with those who did not have early readmission (Table 1). Scheduled follow-up within 14 days and 30 days of discharge was similar between patients readmitted within 30 days and those not readmitted (52 vs. 53%, *P* = 0.67 and 77 vs. 73%, *P* = 0.24, respectively). Of the patients with early readmission, only 115 (35%) were seen in their primary care physician's office prior to readmission/emergency department visit.

Glucose therapy intensification occurred in 227 (12%) patients, whereas glucose therapy de-intensification occurred in 405 (21%) patients (Table 2). At the time of discharge, 15% of diabetes-related medication-naïve patients at the time of admission were started on new diabetes medications. Insulin was started in 5% (63/1275) of previously insulin-naïve patients and oral agents were started in 5% (30/554) of previously oral-agent-naïve patients. Of patients on diabetes medication before admission, at least one diabetes medication was discontinued in 40% of patients at discharge; oral agents were stopped in 27% (377/1395) and insulin stopped in 10% (69/674) of patients during the index admission. Similarly, intensification of anti-hypertensive regimens occurred in 113 (6%) patients, whereas de-intensification occurred in 524 (27%). Thirty-two patients had intensification of both diabetes and anti-hypertensive medications. Three quarters of the patients (1467, 75%) were on statins and 320 (16%) were on glucocorticoids at the time of admission. Only 140 (7%) had changes to statin medications, the majority (*n* = 123) with discontinuation.

There were no statistically significant differences in race, admitting service, prevalence of congestive heart failure or diabetes as primary reason for admission. Diabetes was listed as

the primary reason for early hospital readmission in six patients (two had glucose therapy de-intensification, four no change, none with glucose therapy intensification during their index admission) and hypoglycaemia was the primary reason for emergency department admission in five patients (only one with glucose therapy intensification at index admission).

Medication intensification and readmission risk

In univariate analyses (Table 2), diabetes medication regimen intensification was not associated with early hospital readmission or emergency department admission (odds ratio 0.94, 95% CI 0.64–1.37, $P = 0.74$). Similarly, we found no significant differences in rates of angiotensin-converting enzyme inhibitor/angiotensin receptor blocker or statin use, or rates of anti-hypertensive medication regimen intensification by early readmission status.

In the pre-specified analysis of 399 medicine patients with poorly controlled glycaemia prior to admission (baseline HbA_{1c} ≥ 64 mmol/mol), 73 (18%) had glucose therapy intensification, 73 (18%) had glucose therapy de-intensification and 253 (65%) had no change (Table 3). In multivariate logistic regression models, diabetes regimen intensification during hospitalization was associated with a significantly decreased risk of early readmission (odds ratio 0.33, 95% CI 0.12–0.88, $P = 0.03$, Fig. 1) after adjusting for age, index length of stay, discharge home with visiting nurse services, 'primary care physician connectedness', baseline HbA_{1c} and Charlson co-morbidity score. In contrast, similar multivariate logistic regression models of diabetes regimen de-intensification (odds ratio 1.28, 95% CI 0.60–2.72, $P = 0.53$) and intensification (odds ratio 1.40, 95% CI 0.86–2.40, $P = 0.17$) showed no significant association with early readmission or emergency department admission.

Post-discharge glycaemic control

Follow-up HbA_{1c} was available for 368 of the 399 (92%) medicine service patients with baseline HbA_{1c} ≥ 64 mmol/mol (8%). After approximately 3 months post-discharge [mean days (SD): 93 (66) vs. 96 (84) vs. 99 (72) days for glucose therapy intensification, glucose therapy de-intensification and no significant change groups respectively, $P = 0.80$], patients with glucose therapy intensification had a significantly greater decrease in baseline HbA_{1c} level compared with patients with glucose therapy de-intensification {mean HbA_{1c} decrease (SD): 20 (26) mmol/mol [1.8 (2.4) %] vs. 7 (15) mmol/mol [0.6 (1.4) %], $P < 0.01$ }; this difference was not different compared with patients with no change {15 (26) mmol/mol [1.4 (2.4) %], $P = 0.19$ }.

Discussion

Among primary care patients with Type 2 diabetes admitted to a large academic hospital, glucose therapy intensification was not associated with an increased risk of 30-day unplanned readmission or emergency department admission. Indeed, among patients with poorly controlled diabetes admitted to the medicine service, intensification was associated with decreased risk of 30-day readmission/emergency department admission and was associated with greater improvement in HbA_{1c} after discharge. The results of our study support diabetes regimen optimization during the hospital admission as both a safe and effective approach to improving short-term outcomes and achieving longer-term outpatient glycaemic control.

This study reinforces the idea that hospitalization is a 'teachable moment' for intensification of diabetes care in patients with poor glycaemic control (HbA_{1c} ≥ 64 mmol/mol), regardless of reason for admission. Intensifying glucose therapy during hospitalization with planned continuation at discharge has several advantages. Such intensification may help focus the patient and their family/care provider(s) on the risk of diabetes-related complications and

strengthen the perception that therapy is an essential part of the patient's long-term care. Furthermore, the more intensive monitoring and localization of expertise of nurses, pharmacists, nutritionist and diabetes educators within the hospital setting may provide a safer environment for insulin initiation and rapid dose titration. Additional studies of the transition between hospital and home, in particular studying the durability of medication changes and diabetes-related self-care efforts after discharge, as well as impact of interventions to improve self-care and glycaemic control in this transition period, are needed.

The overall lack of association between changes in diabetes medications and 30-day outcome in the overall cohort may reflect differences in indication for medication changes based on baseline HbA_{1c}, nutritional status during hospitalization and the practice patterns of different hospital services. Routine discontinuation of oral agents is appropriate in anticipation of nutritional changes or procedures (i.e. computed tomography scans with contrast). Failure to restart medication at the time of discharge has been associated with increased adverse outcomes in acute myocardial infarction patients [23] and thus should be more closely evaluated in future studies. Changes to medication regimens in the surgical population are harder to interpret as procedures and their complications may dramatically alter glycaemic control (e.g. gastric bypass, gastrointestinal tract resections, post-transplant immunosuppression). For these reasons, we limited the sub-analysis to medicine service patients with baseline HbA_{1c} 3–64 mmol/mol (8%). It is in this population that we see a significant association between intensification of diabetes regimens and decreased risk for 30-day unplanned readmission/emergency department visit.

These results must be considered within the limitations of the study design. This was an observational study and limited to patients discharged home who received their care at a single large tertiary-care hospital and its associated outpatient clinics, and may therefore not be generalizable to other settings. Although admissions or emergency department visits at other institutions were not captured, the patients we studied all receive their primary care within our care network, and would most likely to be brought to Massachusetts General Hospital for emergency and hospital-level care. While there is likely a small number of patients admitted elsewhere, these missing outcomes are not likely to occur preferentially in one vs. the other of the exposure categories and thus are not expected to systematically bias our results.

The focus of our analysis was primarily on major diabetes medication changes (initiation or discontinuation), and thus dose changes within a drug class, pre- and post-hospitalization adherence to medication regimens and endocrine consultation in either inpatient or outpatient care were not assessed. Inpatient glycaemic control or rates of hypoglycaemia during hospitalization, which could influence glucose therapy titration during hospitalization, were also not available. Conversely, the use of electronic admission and reconciled discharge medication orders represents a strength of the study. Finally, although we cannot impute any causality in this observational study, and the differences in readmission rate could reflect some non-specific beneficial effect of intensification of therapy, such as closer clinical contact and attention from inpatient providers, the absence of any effect on readmission of the intensification of blood pressure or lipid therapy suggests otherwise.

With healthcare delivery systems focused on improving patient quality of care and outcomes without increasing healthcare cost, comprehensive treatment of chronic conditions such as diabetes during hospitalization may become an important goal for hospitals within care systems that are held accountable for the post-discharge outcome of their patients. One growing model to improve inpatient diabetes care is the establishment of diabetes inpatient

specialty nurses/teams for patient education and medication titration, which has already been shown to reduce length of stay in hospitalized patients [24–26]. Post-discharge glycaemic control outcomes have not been assessed. The findings in this study of intensification of diabetes medication regimens in poorly controlled patients being associated with both decreased risk for early re-hospitalization and with improved HbA_{1c} control 3 months after discharge is novel and adds to the discussion about future development and study of inpatient diabetes management models. Whether this relationship is causal or a marker for other effective care practices, such as better discharge medication reconciliation and discharge planning, is not known and warrants future research as we strive to improve overall healthcare while reducing cost.

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Figure 1.
Adjusted risk of 30-day readmission/emergency department visit (C-statistic 0.695)

Table 1
Comparison of patient characteristics with and without 30-day unplanned hospital readmission or emergency department admission

	All patients (<i>n</i> = 1949)		Medicine only, baseline HbA _{1c} 64 mmol/mol (<i>n</i> = 399)	
	30-day outcome <i>n</i> = 324 (17%)	No outcome <i>n</i> = 1625 (83%)	30-day outcome <i>n</i> = 56 (14%)	No outcome <i>n</i> = 343 (86%)
Male, <i>n</i> (%)	188 (58)	835 (52)	32 (57)	186 (54)
Age, mean (SD), years	66 (13)	65 (13)	59 (15)	60 (14)
White race, <i>n</i> (%)	237 (73)	1,204 (74)	37 (66)	222 (65)
Medicine service, <i>n</i> (%)	238 (73)	1,176 (72)	0.73	0.88
High primary care physician connectedness, <i>n</i> (%)	246 (76)	1,316 (81)	0.04	0.08
Charlson co-morbidity score, mean (SD)	3.0 (2.0)	2.8 (1.8)	0.02	0.33
Baseline HbA _{1c} *, mean (SD) mmol/mol	57 (17)	60 (20)	0.18	0.19
%	7.4 (1.6)	7.6 (1.8)	9.6 (1.8)	10 (1.9)
Length of stay, mean (SD) days	5.0 (4.4)	3.9 (3.3)	5.9 (4.6)	4.3 (3.4)
Diabetes as primary admission diagnosis, <i>n</i> (%)	20 (6)	97 (6)	7 (12)	59 (17)
Visiting nurse association services, <i>n</i> (%)	124 (38)	517 (32)	0.03	0.20

* Missing 65 baseline HbA_{1c} values, 18 from 30-day outcome group.

Table 2

Comparison of admission diabetes medications and changes to diabetes medication regimens in patients with and without 30-day unplanned readmission or emergency department admission

	All patients (<i>n</i>)		Medicine only, baseline HbA _{1c} 64 mmol/mol (<i>n</i> = 399)		<i>P</i> -value
	30-day outcome <i>n</i> = 324 (17%)	No outcome <i>n</i> = 1949	30-day outcome <i>n</i> = 56 (14%)	No outcome <i>n</i> = 343 (86%)	
Intensification	36 (11)	191 (12)	5 (9)	68 (20)	0.06
De-intensification	74 (23)	331 (20)	11 (20)	62 (18)	0.85
No diabetes medication on admission	36 (11)	256 (16)	1 (2)	19 (6)	0.33
Insulin, <i>n</i> (%) on at admission	112 (35)	562 (35)	33 (60)	218 (64)	0.55
New start insulin, <i>n</i> (%) [*]	9 (4)	54 (5)	2 (9)	20 (16)	0.53
Oral agent, <i>n</i> (%) on at admission	241 (74)	1,154 (71)	46 (82)	248 (72)	0.14
Oral agent stopped, <i>n</i> (%) [†]	66 (27)	311 (27)	14 (30)	72 (29)	0.86

^{*} As a percentage of patients not on insulin at the time of admission.

[†] As a percentage of patients on oral agents at the time of admission.

Table 3

Baseline characteristics for poorly controlled (baseline HbA_{1c} ≥ 64 mmol/mol) patients on the medicine service stratified by changes in diabetes medication regimens

	Intensification of diabetes medications <i>n</i> = 73 (18%)	De-intensification of diabetes medications <i>n</i> = 73 (18%)	No significant change of diabetes medications <i>n</i> = 253 (64%)	<i>P</i> -value
Male, <i>n</i> (%)	37 (51)	42 (58)	139 (55)	0.70
Age, mean (SD)	57 (14)	65 (13)	59 (14)	< 0.01 [*]
White, <i>n</i> (%)	42 (58)	49 (67)	168 (69)	0.34
Charlson co-morbidity score, mean (SD)	2.6 (1.7)	3.3 (2.1)	2.5 (1.6)	< 0.01 [*]
High primary care physician connectedness, <i>n</i> (%)	53 (73)	58 (79)	174 (69)	0.20
Baseline HbA _{1c} , mean (SD) mmol/mol	89 (22)	79 (16)	86 (21)	0.03 [†]
%	10.3 (2.0)	9.4 (1.5)	10 (1.9)	
Index length of stay, mean (SD)	5.6 (4.4)	4.1 (3.1)	4.3 (3.5)	0.02 [‡]
Diabetes as primary admission diagnosis, <i>n</i> (%)	16 (22)	10 (14)	40 (16)	0.36
Visiting nurse association services	22 (30)	21 (29)	69 (27)	0.88
30-day outcome, <i>n</i> (%)	5 (7)	11 (15)	41 (16)	0.07

^{*} Significant difference between de-intensification and no change subgroups.

[†] Significant difference between intensification and de-intensification subgroups.

[‡] Significant difference between intensification and both de-intensification and no change subgroups.