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Use of Intensive Glycemic Management in Older Adults with Diabetes

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Abstract

Background: Tight glucose control reduces microvascular complications at the cost of an increased risk of hypoglycemia. Guidelines recommend conservative management for older adults with diabetes, particularly in the setting of comorbidities. We examined the proportion of older adults with diabetes treated with tight glucose control and the factors associated with this practice.

Design/Setting/Participants: Cross-sectional analysis of 42,669 adults 75 years of age with type 2 diabetes from 151 US outpatient sites in the Diabetes Collaborative Registry.

Measurements: Patients were categorized based on HbA1c and glucose-lowering medications: poor control (HbA1c >9%), moderate control (HbA1c >8–9%), conservative control (HbA1c 7–8%), tight control (HbA1c <7%) with low-risk agents (low risk for hypoglycemia), tight control with high-risk agents, and diet control (HbA1c <7% on no glucose-lowering medications). We used hierarchical logistic regression to examine patient and site factors associated with tight control/high-risk agents vs. conservative control or tight control/low-risk agents.

Results: Among 30,696 patients without diet controlled diabetes, 5,596 (18%) had moderate or poor control, 9,227 (30%) had conservative control, 7,893 (26%) had tight control on low-risk agents, and 7,980 (26%) had tight control on high-risk agents. Older age, male sex, heart failure,

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AUTHOR CONTRIBUTIONS:

SVA and JW had full access to the data and take responsibility for the integrity of the data and the accuracy of the data analysis. SVA conceived of the study idea, developed the analytic framework, and directed the analysis. SVA, SNM, and MK acquired the data. JW performed statistical analysis. SVA, KJL, JW, LS, SNM, and MK made important intellectual contributions to analytic design and interpretation of the results. SVA drafted the manuscript. KJL, JW, LS, SNM, and MK provided critical revision of the manuscript for important intellectual content.

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chronic kidney disease, and coronary artery disease were each independently associated with a greater odds of tight control with high-risk agents. There were no differences among practice specialties (endocrinology, primary care, cardiology) in how aggressively the patients were managed.

Conclusion: We found that a quarter of US older adults with type 2 diabetes are tightly controlled with glucose-lowering medications that have a high risk of hypoglycemia. These results suggest potential overtreatment of a substantial proportion of patients and should encourage further efforts to translate guidelines to daily practice.

Keywords

diabetes mellitus; glucose control; hypoglycemia

The epidemic growth of diabetes in the US has been driven largely by the aging of the population, where it is estimated that 26% of adults 65 years of age have diabetes.¹ Glycemic management in older adults, however, has unique challenges. Tight glucose control reduces the risk of microvascular complications,² but these potential benefits are counterbalanced by increased episodes of hypoglycemia that are a natural consequence of tight glucose control, particularly with the use of insulin-providing medications. As older adults are less likely to benefit and more likely to be harmed from tight glucose control, the American Diabetes Association guidelines have suggested, at least since 2004, that treatment targets should be relaxed in older patients with diabetes, with particular attention to minimize hypoglycemia.^{3, 4} After the ACCORD trial showed an increase in mortality with intensive glucose control,⁵ the Veterans Administration in 2010⁶ and the European Diabetes Working Party for Older People in 2011⁷ also recommended higher HbA1c targets in older adults with diabetes, with the American Diabetes Association further strengthening their recommendation in 2012.¹ However, prior studies have shown that this guidance has not translated effectively to clinical practice, with frequent use of intensive management in older adults with diabetes.^{8–10} Over the last decade, there has been a marked increase in the number of glucose-lowering medications that confer negligible risk for hypoglycemia, expanding the menu of safer treatment options. In order to investigate whether these newer treatment options, along with updated guideline statements,^{4, 6, 7} have shifted glucose management of older patients, we used a large US outpatient database of adults with diabetes to examine contemporary practice patterns of glycemic control and to examine patient factors that might contribute to these treatment choices.

METHODS

Patient Population.

DCR is a US quality improvement registry that was designed to describe the outpatient care of diabetes through the spectrum of primary and specialty care.¹¹ Patient data are extracted from electronic health records using an automated system integration solution. Data were examined from 2014–2016 with the most recent visit used for each patient. The present analyses were limited to patients 75 years of age with type 2 diabetes and available HbA1c data. Because participation in the registry requires no data collection beyond that of the

routine clinical care and all collected data are de-identified, a waiver of written informed consent and authorization for this study was granted by Chesapeake Research Review Incorporated.

Statistical Analysis.

Patients were divided into categories of glycemic management: diet control (HbA1c <7% on no glucose-lowering medications), tight control with high-risk agents (HbA1c <7% on insulin, sulfonylurea, or meglitinides), tight control with low-risk agents (HbA1c <7% on medications with low risk for hypoglycemia: metformin, dipeptidyl peptidase 4 inhibitors, thiazolidinedione, sodium-glucose co-transporter 2 inhibitors, glucagon-like peptide-1 receptor agonists, alpha-glucosidase inhibitors, colesevelam, and/or bromocriptine only [i.e., on no high-risk medications]), conservative control (HbA1c 7–8%), moderate control (HbA1c >8 to 9%), and poor control (HbA1c >9%). We compared demographic and clinical factors among these groups using chi-square tests for categorical variables and one-way ANOVA for continuous variables.

We used multivariable hierarchical logistic regression to examine factors associated with tight control with high-risk agents. For this analysis, we excluded patients with diet control and moderate/poor control. Covariates in the model included age, sex, heart failure, chronic kidney disease (glomerular filtration rate <30 mL/min/1.83 m², dialysis, or [if glomerular filtration rate unavailable] a chart diagnosis of chronic kidney disease), coronary artery disease, and site specialty (endocrinology, cardiology, primary care). Site was included as a random effect, to account for patient clustering within sites. All analyses were performed with SAS version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

Among 42,669 patients with type 2 diabetes who were 75 years of age, 11,973 (28.1%) patients had diet-controlled diabetes, 15,873 (37.2%) had tight control, 9,227 (21.6%) had conservative control, 2,750 (6.4%) had moderate control, and 2,846 (6.7%) had poor control. Among patients with tight control, half were treated with medications with a high risk of hypoglycemia (26% of all patients not diet-controlled). Patients treated by endocrinologists were less likely to have poor glycemic control, and patients treated by primary care physicians were more likely to be conservatively managed (Figure 1).

Patients with tight control on high-risk agents were notably older and had a high burden of comorbidities (Table 1). Patients in this group were treated with an average of 1.9 ± 0.9 glucose-lowering medications, and mean HbA1c was $6.3\% \pm 0.4\%$. Patients treated with tight control with low-risk agents were on an average of 1.2 ± 0.5 glucose-lowering medications, which was most often metformin in 86.2%. In the multivariable model, older age, male sex, heart failure, chronic kidney disease, and coronary artery disease were each independently associated with a greater odds of tight control with high-risk agents (Figure 2). After adjusting for these patient factors, there were no differences among specialties in how aggressively the patients were managed ($p=0.398$).

DISCUSSION

In a large US outpatient cohort, we found that a quarter of older adults with type 2 diabetes that was not controlled with diet alone were managed with tight control on medications that have a high risk of hypoglycemia. Contrary to expectations, older age and comorbidities were associated with a higher likelihood of tight glucose management with high-risk agents, which runs counter to guideline recommendations for more conservative management in these patients.^{4, 6, 7} Despite greater availability of agents that do not typically cause hypoglycemia, insulin or insulin secretagogues continue to be used at high rates in older adults, even when HbA1c levels are low. These results suggest potential overtreatment of a substantial proportion of older patients with diabetes.

When managing risk factors, physicians often focus on achieving particular targets (e.g., HbA1c, blood pressure, cholesterol). However, it is important to recognize that older patients may not derive the same benefits from risk factor control as younger patients—especially when the risk factor takes years to exert its influence on patient outcomes, while treatment of the risk factor has immediate potential for harm. It is for this reason that most of risk factor quality metrics do not apply to patients 75 years of age, although many providers are unaware of this distinction or are fearful to cause harm or even be exposed to liability if they de-escalate therapy in older adults.¹² Tight glucose control reduces the risk of microvascular (and perhaps macrovascular) events; however, it likely takes >10 years of tight glycemic control to realize any benefit.² On the other hand, tight glucose control markedly increases the risk of hypoglycemia—a risk that is even greater in older adults who have defective glucose counter-regulation, multiple comorbidities, and polypharmacy.¹³ Hypoglycemia is not just a benign nuisance, but is associated with an increased risk of myocardial infarction, heart failure, stroke, cardiovascular death,¹⁴ falls, fracture, and dementia, in addition to its adverse effects on quality of life and increased healthcare costs.^{13, 15}

Our data show that efforts are needed to more efficiently translate the guideline recommendations to daily practice. Busy healthcare providers may be challenged to identify optimal diabetes treatment strategies in older adults with multiple comorbidities, given the need to address numerous, frequently revised evidence-based guidelines and quality metrics. This is even more challenging when de-escalation is the evidence-based recommendation, as guidelines often use vague or cautionary language (e.g., “glycemic goals for some older adults might be reasonably relaxed, using individual criteria”). Furthermore, while quality metrics for risk factor management often do not apply to older adults, there are no incentives or specific metrics to cut back on therapy. Future work should focus on generating better evidence on when, how, in whom to de-intensify and on assuring that incentives align with these recommendations.

There are potential limitations to our work that should be considered. First, as all DCR sites are voluntarily participating in the registry, which is designed for quality improvement, our results may not represent general care of patients with diabetes in the US. Second, it is possible that other factors may justify tight control in some of the older patients in this study, which may include longer life expectancy despite the presence of comorbidities and patient

values and preferences about treatment. Third, the higher use of insulin and sulfonylureas in patients with comorbidities may reflect potential concerns about cardiac or renal safety with both metformin and the emerging medications (even though several of these medications have demonstrated cardiovascular and nephroprotective benefits across the range of age, comorbidity burden, and moderate chronic kidney disease). However, while providers might be uncomfortable using these classes of medications in older patients with comorbidities, this does not explain why these patients are treated to a low HbA1c target. In patients who may only be eligible for glucose-lowering medications with higher risk of hypoglycemia, conservative glycemic targets are even more important. Finally, we were unable to identify harms of tight control with high-risk agents, as hypoglycemia events are poorly captured in outpatient electronic health records.

In conclusion, we found that 26% of older adults with diabetes that was not controlled with diet alone had HbA1c levels <7% while being treated with medications that have high risk for hypoglycemia. Despite evidence of increased risk of harm without substantial clinical benefit, it appears that tight glycemic control with high-risk agents remains prevalent among older patients with multiple comorbidities. Further efforts are needed to provide more specific guidance on how to safely treat older adults with diabetes (both through targeting treatment with low-risk agents and through de-escalation of glucose control) and then to efficiently translate that guidance into busy clinical practice.

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We certify that this work is novel clinical research. The potential impact of this research on clinical care includes the following: recognition of overtreatment of a substantial proportion of older adults with tight glucose control with high-risk agents, which could lead to improved care of these patients through higher HbA1c goals and/or use of glucose-lowering medications with low risk of hypoglycemia.

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Figure 1. Proportions of older adults treated with different categories of glucose control.

Overall and stratified by site specialty. Poor control=HbA1c $\geq 9\%$; moderate control=HbA1c 8 to $<9\%$; conservative control=HbA1c 7 to $<8\%$; tight control/low-risk agents=HbA1c $<7\%$ on only glucose-lowering medications with low risk of hypoglycemia; tight control/high-risk agents=HbA1c $<7\%$ on ≥ 1 glucose-lowering medication with high risk of hypoglycemia. Patients with HbA1c $<7\%$ on diet only were not included.

Figure 2. Patient factors associated with tight glycemic control on high-risk agents. Patients with diet control, moderate control, or poor control were not included in this analysis.

Table 1.

Patient characteristics stratified by glycemic control

Characteristic	Poor control n=2,750	Moderate control n=2,846	Conservative control n=9,227	Tight control/ low-risk agents n=7,893	Tight control/ high-risk agents n=7,980	Diet control n=11,973
Age (years)	81.3±5.0	80.8±4.7	81.2±4.9	80.7±4.7	81.7±5.0	81.9±5.1
Female sex	47.3%	46.0%	44.9%	46.8%	43.4%	51.1%
White race	89.4%	89.0%	89.8%	89.4%	89.1%	90.3%
BMI (kg/m ²)	29.6±6.1	30.4±6.1	29.8±5.7	29.1±5.6	29.6±5.9	28.3±5.5
Smoking history	47.1%	47.6%	47.6%	47.7%	49.5%	46.5%
Hypertension	91.5%	92.3%	90.9%	91.5%	91.6%	92.0%
Systolic BP (mmHg)	129.1±18.9	130.8±18.7	130.3±17.9	129.9±17.5	129.4±18.2	130.5±17.9
Diastolic BP (mmHg)	69.9±10.4	69.8±10.0	70.0±10.0	71.0±9.9	69.2±10.1	71.5±10.0
CKD	12.8%	10.8%	9.4%	4.1%	12.1%	7.4%
CAD	71.9%	71.1%	69.2%	62.4%	70.7%	59.4%
PAD	28.7%	26.4%	24.8%	20.2%	26.6%	22.5%
Prior stroke	16.7%	13.9%	12.6%	12.0%	13.9%	13.1%
Heart failure	41.1%	36.2%	33.4%	25.6%	38.1%	29.4%
Atrial fibrillation	41.2%	36.9%	35.0%	33.1%	38.8%	34.6%
HbA1c (%)	10.6±1.2	8.5±0.3	7.4±0.3	6.2±0.4	6.3±0.4	6.0±0.4
# glucose-lowering medications	1.6±1.3	1.9±1.2	1.7±1.1	1.2±0.5	1.9±0.9	0.0±0.0
Insulin	42.2%	47.0%	29.5%	0.0%	30.9%	NA
Metformin	45.1%	52.2%	54.8%	86.2%	47.9%	NA
Sulfonylurea	39.2%	49.7%	44.4%	0.0%	76.5%	NA
Thiazolidinedione	11.0%	11.1%	9.9%	11.1%	10.9%	NA
DPP-4 inhibitor	17.2%	21.0%	18.7%	17.6%	16.4%	NA
GLP-1 RA	3.3%	4.6%	2.8%	1.6%	2.0%	NA
SGLT2 inhibitor	2.0%	3.6%	2.0%	1.4%	0.9%	NA
Other medications	4.3%	4.7%	4.3%	2.8%	6.6%	NA

BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; CAD, coronary artery disease; PAD, peripheral artery disease; DPP-4, dipeptidyl peptidase-4; GLP-1 RA, glucagon-like peptide-1 receptor agonist; SGLT2, sodium-glucose co-transporter 2

P<0.001 for all comparisons except White race (p=0.112) and hypertension (p=0.054)