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Comparison of Efficacy and Safety of Glargine and Detemir Insulin in the Management of Inpatient Hyperglycemia and Diabetes

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Abstract

Objective—Glargine and detemir insulin are the two most commonly prescribed basal insulin analogs for the ambulatory and inpatient management of diabetes. The efficacy and safety of basal insulin analogs in the hospital setting has not been established.

Methods—This observational study compared differences in glycemic control and outcomes in non-ICU patients with blood glucose (BG) >140 mg/dl who were treated with glargine or detemir, between 01/01/2012 and 09/30/2015 in two academic centers.

Results—Among 6,245 medical and surgical patients with hyperglycemia, 5,749 received 1 dose of glargine and 496 patients received detemir during the hospital stay. There were no differences in the mean daily BG (glargine 182±46 mg/dl and detemir 180±44 mg/dl, $p=0.70$). There were no differences in mortality, hospital complications, or readmissions between groups (all, $p=NS$). After adjusting for potential confounders, there was no statistically significant difference in hypoglycemia rates between treatment groups. Patients treated with detemir also required higher total daily basal insulin doses (0.27 ± 0.16 vs 0.22 ± 0.15 units/kg/day, $p<0.001$). Glargine-treated patients had statistically longer LOS, however this difference may not be clinically relevant [6.8 ± 7.4 vs 6.0 ± 6.3 days, $p<0.001$].

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Conclusions—Our study indicates that treatment with glargine and detemir resulted in similar inpatient glycemic control in general medicine and surgery patients. Detemir treatment was associated with higher daily basal insulin dose and number of injections. A prospective randomized study is needed to confirm these findings.

Introduction

Hyperglycemia is common among hospitalized patients, affecting up to one-third of patients admitted to non-ICU settings (1, 2). Hyperglycemia has been associated with increased risk of hospital-related complications in patients with or without diabetes (3, 4). Improved glycemic control reduces hospital-related outcomes, such as infections and length-of-hospital stay (LOS) (5). National clinical guidelines recommend the use of basal insulin plus rapid acting insulin before meals as the treatment of choice for the management of hyperglycemia and diabetes in most non-ICU patients (6–8). Several randomized controlled trials using subcutaneous basal-bolus insulin regimens have reported better glycemic control and reduction of complications with this approach compared to sliding-scale insulin in patients with type 2 diabetes (9–11). Insulin glargine and detemir are the most commonly used basal insulin formulations, and have been associated with lower glycemic variability and less severe hypoglycemia compared to neutral protamine hagedorn insulin (NPH) or premixed insulin formulations (12–14).

A large number of studies in patients with type 2 diabetes (13, 15–18) and a Cochrane meta-analysis (19) have reported minor differences in pharmacodynamics and improvements in glycemic control with the use of glargine and detemir in ambulatory settings. Studies in ambulatory patients have consistently reported similar improvement in glycosylated hemoglobin (HbA1c) and fasting plasma glucose with these two basal insulin analogs (16, 17, 19), with some studies reporting higher daily insulin requirements in patients treated with detemir insulin (18, 19). Despite the extensive data from ambulatory studies, few studies have compared the efficacy of glargine and detemir insulin in the hospital setting (20, 21). Accordingly, this study aimed to compare the efficacy and safety of the two most commonly used basal insulin formulations in the management of inpatient hyperglycemia and diabetes in non-ICU settings.

Materials and Methods

Sites and study population

In this retrospective analysis, we included patients older than 18 years of age, with admission BG between 140 and 400 mg/dl, and who were treated with glargine or detemir during their hospitalization. The patient population included general medicine and surgery patients admitted to The Mount Sinai Hospital in New York and Emory University Hospital, Emory University Midtown Hospital, Emory Saint Joseph's and Emory Johns Creek Hospitals in Atlanta. Patients hospitalized at Emory Hospitals between 01/01/2012 to 09/30/2015, and patients hospitalized at The Mount Sinai Hospital between 01/01/2015 to 09/30/2015 were included in the study. We excluded patients admitted to the ICU, patients with ICD-9 diagnoses for diabetic ketoacidosis, hyperosmolar hyperglycemic state, and

pregnancy. The study was approved by the Institutional Review Board at both The Mount Sinai School of Medicine and Emory University.

Protocols for management of hyperglycemia and hypoglycemia

Mount Sinai and Emory have protocols for the management of hyperglycemia in hospitalized non-critically ill patients with diabetes. The protocols recommend a basal-bolus subcutaneous insulin regimen, targeting a fasting/pre-meal BG < 140 mg/dl and a random BG < 180 mg/dl. Insulin glargine was the preferred formulary basal insulin in the two institutions but both detemir and NPH were available in the order entry systems. Similarly, both institutions have protocols for the management of hypoglycemia, starting therapy for BG < 70 mg/dl at that time (6, 7).

Data acquisition

De-identified data was collected from the Mount Sinai and Emory University Clinical Data Warehouse. Both systems collect data from the hospital electronic medical records, billing systems and laboratory and pathology departments. The diagnosis of diabetes, co-morbidities on admission, and hospital complications were identified by ICD-9 codes, generated during the hospitalization. ICD-9 codes were collected for patient's comorbidities present on admission. These codes were used to calculate the Charlson comorbidity score, a previously validated score that has been shown to correlate with outcomes (22). ICD-9 codes generated during the hospital stay, but not present during admission, were used to calculate the rate of complications. Blood glucose values included point-of-care testing and laboratory glucose measures.

Study Outcomes

The primary outcome was to determine differences in glycemic control, defined as mean daily blood glucose concentration between glargine and detemir-treated patients. Secondary outcomes included differences in the frequency of hypoglycemia < 70 mg/dl and severe hypoglycemia < 40 mg/dl at any time of the day and nocturnal hypoglycemia between midnight to 06:00 AM. Other secondary outcomes included frequency of severe hyperglycemia > 250 mg/dl, maximum daily glucose concentration, hospital length-of-stay and 30-days readmission rates between patients treated with glargine and detemir. We also compared differences in the number of insulin injections per day and the total daily basal insulin dose administered in units/kg/day of glargine and detemir. Furthermore, we compared differences in a composite of complications including hospital mortality, major adverse cardiovascular events, acute respiratory failure, acute kidney injury, bacteremia, pneumonia, post-operative wound infection, and cerebro-vascular accidents. We also compared differences between groups on glycemic control and hypoglycemia in patients with renal dysfunction, defined as an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m² on admission or during the hospital stay.

Statistical methods

We conducted univariate analyses to compare patient demographics and clinical characteristics and outcomes between patients treated with glargine or detemir during the

hospital stay. We summarized continuous variables by mean $\pm$ standard deviation (SD) or median with interquartile range (IQR) when skewness was present, and discrete variables by frequency (relative frequency). We compared continuous variables based on nonparametric Kruskal-Wallis tests. For categorical variables, we used Chi-square tests or Fisher's exact tests when needed. We also performed multivariate analyses to assess the effect of treatment on hospital LOS, hypoglycemia and glycemic control while adjusting for various potential confounders. For the binary outcomes, we employed logistic regression. In the multivariate models, we analyzed interaction terms between significantly different variables identified in univariate analysis and we excluded them from the final analysis when they were found to be insignificant. A p value < 0.05 was considered as significant. Statistical analysis was performed using SAS (version 9.3).

Results

A total of 6,245 patients with hyperglycemia were included; of them, 5,749 (92%) patients were treated with glargine and 496 (8%) were treated with detemir insulin. Demographic and clinical characteristics of the study population are shown in Table 1. A total of 78% of patients in the glargine and 73% in the detemir group had a known history of diabetes prior to admission. Treatment groups were similar with no differences in mean age (63.3 ± 13 vs 63.2 ± 13 years, $p = 0.92$), body mass index (BMI 30.7 ± 7 vs 30.9 ± 7 kg/m², $p = 0.31$), mean admission HbA1c ($8.2\% \pm 2.1$ [66.1 mmol/mol] vs $8.2\% \pm 1.8$ [66.1 mmol/mol], $p = 0.60$) or mean glomerular filtration rate (eGFR 60 ± 34 vs 59 ± 34 ml/min/1.73 m², $p = 0.18$). Charlson score was marginally higher in the detemir group (2.0, [IQR] 2–3) than in the glargine group (2.0, [IQR] 2–4, $p = < 0.001$). There were no differences in the number of patients with eGFR < 60 ml/min/1.73 m² (63.5% vs 67.1%, $p = 0.15$) and eGFR < 30 ml/min/1.73 m² (23% vs 23.7% ($p = 0.72$) in patients treated with glargine and detemir, respectively.

There were no differences in the mean-hospital BG (182 ± 46 mg/dl vs 180 ± 44 mg/dl, $p = 0.70$), number of patients with severe hyperglycemia, BG > 250 mg/dl (70% vs 69%, $p = 0.56$), or in the maximum BG during the first 48-hours (271 ± 89 mg/dl vs 264 ± 85 mg/dl, $p = 0.16$) between patients treated with glargine and detemir, respectively (Table 2). Differences in mean daily hospital BG between groups are shown in Figure 1.

The overall rate of hypoglycemia was higher in the detemir-treated group (33.5% vs 29%, $p = 0.03$). However, there were no differences in the rate of severe hypoglycemia (5% vs 5.2%, $p = 0.80$) or nocturnal hypoglycemia between midnight and 06:00 AM (10% vs. 11%, $p = 0.47$) between glargine and detemir groups, Table 2. In multivariate analyses, there was no difference in frequency of hypoglycemia between groups after adjusting for age, race, gender, BMI, admission service, and admission HbA1c (odds ratio [OR] 1.2, 95% CI 0.9 – 1.6, $p = 0.32$). In a subgroup analyses of patients with impaired kidney function and eGFR < 60 ml/min/1.73 m², there were no differences in mean daily BG (178.1 ± 45.2 mg/dl vs 176.7 ± 42.7 mg/dl, $p = 0.70$) or in the rate of hypoglycemia (35.1% vs 41%, $p = 0.067$) between glargine and detemir groups.

The total daily basal insulin dose was higher in patients treated with detemir (0.27 ± 0.16 units/kg) compared to those treated with glargine (0.22 ± 0.15 units/kg), $p < 0.001$. In

addition, patients treated with detemir received more daily insulin injections (1.14 ± 0.28 vs 1.07 ± 0.20 , $p = 0.001$) compared to patients treated with glargine insulin.

There were no differences in hospital mortality (1.2% vs. 0.4%, $p=0.12$) or in the frequency of hospital readmissions (3.3% vs. 4.6%, $p=0.13$) between patients treated with glargine and detemir, respectively. In addition, there were no differences in the composite of complications that included in-hospital mortality, major adverse cardiovascular events, cerebrovascular events, acute kidney injury, acute respiratory failure, pneumonia, bacteremia, or post-operative wound infection (42% vs 42%, $p=0.89$), as shown in Table 2.

We observed a longer mean hospital LOS in the glargine group [6.8 ± 7.4 vs 6.0 ± 6.3 days, $p < 0.001$]. In multivariate linear regression analysis, we found that age, BMI, admission HbA1c and Charlson comorbidity score were predictors of hospital LOS. After adjusting for these factors, treatment with glargine remained significantly associated with longer LOS compared to detemir, $p=0.001$.

To further investigate potential differences on efficacy and safety of these basal insulin analogs we performed multivariate analyses adjusting for several clinical variables, including statistically significant interactions. Defining a good treatment response in glycemic control as all BG between 70 and 180 mg/dl during the hospital stay, there were no differences in response (OR 1.4, 95% CI 0.7–2.6, $p=0.33$) to glargine or detemir after adjusting for age, race, gender, BMI, admission service and admission HbA1c. In a subgroup analysis of patients with impaired renal function ($eGFR < 60$ ml/min/1.73 m²), we observed no difference in good treatment response in glycemic control (OR=2.2, 95% CI: 0.98–4.8; $p=0.057$) or in odds of hypoglycemia between glargine and detemir (OR=1.1, 95% CI: 0.8–1.7; $p=0.57$).

Discussion

This study compared the efficacy and safety of the two most commonly prescribed basal insulin formulations -glargine and detemir- for the management of hospitalized patients with hyperglycemia and diabetes in non-ICU settings. Our results show that treatment with glargine and detemir result in similar glycemic control without differences in hospital mortality, hospital complications, and hospital readmissions. Treatment with detemir was associated with slightly higher rates of hypoglycemia, total daily basal insulin dose and number of injections per day, but was associated with a marginally shorter hospital LOS compared to patients treated with insulin glargine.

Clinical guidelines from professional organizations have recommended the use of subcutaneous (SQ) insulin as the preferred therapy for glycemic control in hospitalized patients in non-critical settings (6–8). The results of several randomized controlled trials have shown that treatment with basal-bolus regimens with insulin analogs improves glycemic control and reduces the rate of hospital complications in patients with T2D compared to sliding-scale insulin regimens (9–11). In addition, the use of basal insulin analogs results in similar glycemic control but in lower rates of hypoglycemia in hospitalized patients with type 1 and type 2 diabetes compared to treatment with NPH (12,

23) and premixed insulin formulations (14). Based on these studies, the use of basal insulin analogs -glargine and detemir- has become the preferred insulin formulations in the hospital setting. Two studies have compared treatment with glargine and detemir in the management of hospital hyperglycemia in general medicine and surgery patients with type 2 diabetes (20, 21). Zhang et al (20) conducted a short crossover study in 42 patients with type 2 diabetes treated with detemir and glargine insulin. There were no differences in the number of days to achieve target BG (4.0 ± 0.5 days vs. 3.3 ± 0.4 days, $p = 0.286$) or in total daily insulin dose (30.1 ± 2.4 U vs. 30.1 ± 2.9 U, $p = 0.99$) between insulin detemir and insulin glargine. There was no significant difference in the 24-h glucose control or in the frequency of hypoglycemia between groups. Similarly, a study by Ahmad et al (21) in patients undergoing surgery in India, there were no differences in mean daily glucose, hypoglycemia or hospital complications (gastrointestinal and genitourinary) between patients treated with detemir or glargine insulin. In agreement with these studies, patients treated with detemir and glargine in our study had similar glucose control, hospital length-of-stay and complications during the hospitalization. The mean hospital daily BG was just slightly lower than admission BG in both treatment groups, with a standard deviation for the mean hospital BG lower than the admission BG in both groups, suggesting a lower glycemic variability during treatment.

Several clinical studies have reported minor pharmacodynamic and pharmacokinetic differences with the use of glargine and detemir insulin (16, 18, 19). The duration of action of detemir of approximately 18 to 20 hours is slightly shorter than insulin glargine (~ 24 hours), in patients with type 1 and type 2 diabetes using clinically relevant doses of 0.30 – 0.35 units/kg (13, 15). In ambulatory studies, patients treated with detemir insulin required higher total insulin doses compared to glargine insulin, with up to 55–57% of patients requiring twice daily insulin injections (16, 18). In our inpatient study, we observed that treatment with glargine or detemir in hospitalized patients with type 2 diabetes results in similar glycemic control and hospital-related outcomes. Consistent with prior studies, we also observed that patients treated with detemir required higher daily insulin doses and higher number of daily insulin injections compared to glargine insulin.

We observed that patients treated with glargine had a marginally longer LOS compared to those treated with detemir [6.8 ± 7.4 vs 6.0 ± 6.3 days, $p < 0.001$]. However, this small differences may not be clinically relevant. In multivariate analysis; age, BMI, admission HbA1c and disease severity score were found to be significant predictors of hospital LOS. After adjusting for all these factors, treatment with glargine remained significantly associated with longer LOS compared to detemir.

The rate of inpatient hypoglycemia has ranged between 12% and 35% in previous randomized controlled studies with basal-bolus insulin regimen in hospitalized patients (9–12, 14, 24, 25). In the present study, we observed an increased rate of hypoglycemia (33.5% vs. 29%, $p = 0.03$) in patients treated with detemir compared to glargine-treated patients; however, this effect disappeared after adjusting for several variables, suggesting that multiple potential factors could have contribute to this difference. Indeed, we noticed that age, race, gender, BMI, admission service and admission HbA1c are all significant predictors of hypoglycemia. Patients treated with detemir required a higher number of

injections per day (1.14 ± 0.28 vs 1.07 ± 0.20 , $p < 0.001$) and higher insulin dosage in units/kg/day (0.27 ± 0.16 vs 0.22 ± 0.15 , $p < 0.001$) compared to glargine-treated patients. While detemir-treated patients had a higher Charlson co-morbidity score (2.0, IQR 2.0–4.0 vs 2.0 IQR 2.0–3.0, $p < 0.001$), we did not include this variable in our multivariate analysis since it was found to be non-significant ($p = 0.21$).

We investigated differences in the frequency of hypoglycemia in patients with impaired renal function treated with detemir and glargine insulin. Baldwin *et al* reported a higher rate of hypoglycemia in hospitalized patients with type 2 diabetes and renal insufficiency, and that a lower insulin dose of 0.25U/kg/day achieved similar glycemic control with half the rate of hypoglycemia (15.8% vs 30%, $p = 0.08$) compared to the more conventional dose of 0.5U/kg/day (26). In agreement with this report, we found that patients with impaired renal function had an increased risk of hypoglycemia, but there were no differences in hypoglycemia between treatment with glargine and detemir insulin.

We acknowledge several limitations in our analysis, including the small number of patients treated with detemir relative to glargine and the retrospective nature of the study, which limits the ability to accurately differentiate between type 1 and type 2 diabetes or fasting/NPO status. In addition, patients were treated without a single treatment protocol and the starting insulin dose and insulin adjustments were performed as per physician's criteria. In addition, we were not able to collect accurate information on the use of antidiabetic therapy prior to admission. Future randomized controlled studies are needed to compare the safety and efficacy of basal insulin formulations for the treatment of inpatient hyperglycemia.

In summary, our study indicates that general medicine and surgery patients with hyperglycemia or diabetes treated with insulin glargine and detemir achieve similar inpatient glycemic control. Despite small differences in hypoglycemia and daily insulin requirements, both regimens may be appropriate alternatives, and the choice depends on the physician's preferences, costs and hospital formulary options.

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R.J.G and G.E.U designed the study and wrote the manuscript. G.M.D, M.F, D.R.U, F.P, R.T and L.P contributed to the study design, data collection, data analysis and reviewed/edited the manuscript. R.J.G. and G.E.U. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Part of this study was presented orally at the 76th Scientific Sessions of the American Diabetes Association, New Orleans, May 2016.

References

1. Cook CB, Kongable GL, Potter DJ, et al. Inpatient glucose control: a glycemic survey of 126 U.S. hospitals. *Journal of hospital medicine*. 2009; 4:E7–E14.
2. Swanson CM, Potter DJ, Kongable GL, Cook CB. Update on inpatient glycemic control in hospitals in the United States. *Endocr Pract*. 2011; 17:853–61. [PubMed: 21550947]
3. Frisch A, Chandra P, Smiley D, et al. Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. *Diabetes Care*. 2010; 33:1783–8. [PubMed: 20435798]
4. Umpierrez GE, Isaacs SD, Bazargan N, et al. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *The Journal of clinical endocrinology and metabolism*. 2002; 87:978–82. [PubMed: 11889147]

5. Murad MH, Coburn JA, Coto-Yglesias F, et al. Glycemic control in non-critically ill hospitalized patients: a systematic review and meta-analysis. *The Journal of clinical endocrinology and metabolism*. 2012; 97:49–58. [PubMed: 22090269]
6. Umpierrez GE, Hellman R, Korytkowski MT, et al. Management of hyperglycemia in hospitalized patients in non-critical care setting: an endocrine society clinical practice guideline. *The Journal of clinical endocrinology and metabolism*. 2012; 97:16–38. [PubMed: 22223765]
7. Moghissi ES, Korytkowski MT, DiNardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Diabetes Care*. 2009; 32:1119–31. [PubMed: 19429873]
8. Association AD. 13. Diabetes Care in the Hospital, Nursing Home, and Skilled Nursing Facility. *Diabetes Care*. 2017; 38:S80–S5.
9. Umpierrez GE, Smiley D, Zisman A, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes (RABBIT 2 trial). *Diabetes Care*. 2007; 30:2181–6. [PubMed: 17513708]
10. Umpierrez GE, Hor T, Smiley D, et al. Comparison of inpatient insulin regimens with detemir plus aspart versus neutral protamine hagedorn plus regular in medical patients with type 2 diabetes. *The Journal of clinical endocrinology and metabolism*. 2009; 94:564–9. [PubMed: 19017758]
11. Umpierrez GE, Smiley D, Jacobs S, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 surgery). *Diabetes Care*. 2011; 34:256–61. [PubMed: 21228246]
12. Bueno E, Benitez A, Rufinelli JV, et al. Basal-Bolus Regimen with Insulin Analogues Versus Human Insulin in Medical Patients with Type 2 Diabetes: A Randomized Controlled Trial in Latin America. *Endocr Pract*. 2015; 21:807–13. [PubMed: 26121460]
13. Porcellati F, Bolli GB, Fanelli CG. Pharmacokinetics and pharmacodynamics of basal insulins. *Diabetes Technol Ther*. 2011; 13(Suppl 1):S15–24. [PubMed: 21668333]
14. Bellido V, Suarez L, Rodriguez MG, et al. Comparison of Basal-Bolus and Premixed Insulin Regimens in Hospitalized Patients With Type 2 Diabetes. *Diabetes Care*. 2015; 38:2211–6. [PubMed: 26459273]
15. Luzio SD, Dunseath GJ, Atkinson MD, Owens DR. A comparison of the pharmacodynamic profiles of insulin detemir and insulin glargine: a single dose clamp study in people with type 2 diabetes. *Diabetes & metabolism*. 2013; 39:537–42. [PubMed: 24139704]
16. Hollander P, Cooper J, Bregnhøj J, Pedersen CB. A 52-week, multinational, open-label, parallel-group, noninferiority, treat-to-target trial comparing insulin detemir with insulin glargine in a basal-bolus regimen with mealtime insulin aspart in patients with type 2 diabetes. *Clin Ther*. 2008; 30:1976–87. [PubMed: 19108786]
17. Raskin P, Gylvin T, Weng W, Chaykin L. Comparison of insulin detemir and insulin glargine using a basal-bolus regimen in a randomized, controlled clinical study in patients with type 2 diabetes. *Diabetes Metab Res Rev*. 2009; 25:542–8. [PubMed: 19565569]
18. Rosenstock J, Davies M, Home PD, et al. A randomised, 52-week, treat-to-target trial comparing insulin detemir with insulin glargine when administered as add-on to glucose-lowering drugs in insulin-naïve people with type 2 diabetes. *Diabetologia*. 2008; 51:408–16. [PubMed: 18204830]
19. Swinnen SG, Simon AC, Holleman F, Hoekstra JB, Devries JH. Insulin detemir versus insulin glargine for type 2 diabetes mellitus. *The Cochrane database of systematic reviews*. 2011; CD006383. [PubMed: 21735405]
20. Zhang T, Lin M, Li W, et al. Comparison of the Efficacy and Safety of Insulin Detemir and Insulin Glargine in Hospitalized Patients with Type 2 Diabetes: A Randomized Crossover Trial. *Adv Ther*. 2016; 33:178–85. [PubMed: 26809253]
21. Ahmad M, Wafai ZA, Mathur SK, et al. Evaluation of Glycemia Control Achieved by Glargine and Lispro Versus Detemir and Aspart Insulin Regimes in Type 2 Diabetics Undergoing Surgery. *Open Cardiovasc Med J*. 2015; 9:58–61. [PubMed: 26312079]
22. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987; 40:373–83. [PubMed: 3558716]

23. Umpierrez GE, Jones S, Smiley D, et al. Insulin analogs versus human insulin in the treatment of patients with diabetic ketoacidosis: a randomized controlled trial. *Diabetes Care*. 2009; 32:1164–9. [PubMed: 19366972]
24. Boucai L, Southern WN, Zonszein J. Hypoglycemia-associated mortality is not drug-associated but linked to comorbidities. *Am J Med*. 2011; 124:1028–35. [PubMed: 22017781]
25. Farrokhi F, Klindukhova O, Chandra P, et al. Risk factors for inpatient hypoglycemia during subcutaneous insulin therapy in non-critically ill patients with type 2 diabetes. *J Diabetes Sci Technol*. 2012; 6:1022–9. [PubMed: 23063027]
26. Baldwin D, Zander J, Munoz C, et al. A randomized trial of two weight-based doses of insulin glargine and glulisine in hospitalized subjects with type 2 diabetes and renal insufficiency. *Diabetes Care*. 2012; 35:1970–4. [PubMed: 22699288]

Figure 1.
Mean Daily In-Hospital Blood Glucose

Table 1

Demographic and Clinical Characteristics of Study Population.

Characteristic	Glargine	Detemir	p-value
Number of Patients, n (%)	5749 (92)	496 (8)	<0.001
Age, years (mean, SD)	63.3 ± 13.3	63.2 ± 13.0	0.92
Male gender, n (%)	2961 (51.5)	249 (50.2)	0.58
Race, n (%)			0.04
Black	2640 (48.7)	203 (42.8)	
White	2073 (38.2)	198 (41.8)	
Other	707 (13)	73 (15.4)	
BMI, kg/m ² (mean, SD)	30.7 ± 6.9	30.9 ± 6.8	0.31
Diabetes prior to admission, n (%)	4467 (77.7)	362 (73)	0.02
eGFR, mL/min/1.73 m ² (mean, SD)	60.6 ± 34.6	59.3 ± 34.1	0.18
eGFR < 60, mL/min/1.73 m ² (n, %)	3280 (63.5)	285 (67.1)	0.15
eGFR < 45, mL/min/1.73 m ² (n, %)	2223 (39.3)	195 (40)	0.78
eGFR < 30, mL/min/1.73 m ² (n, %)	1340 (23.7)	112 (23)	0.72
Admitting service, n (%)			0.55
Medicine	3991 (69.4)	338 (68.1)	
Surgery	1756 (30.6)	158 (31.9)	
Charlson Score, median (IQR)	2.0 (2.0, 3.0)	2.0 (2.0, 4.0)	<0.001

SD (standard deviation), BMI (body mass index), eGFR (estimated glomerular filtration rate), IQR (interquartile range).

Table 2

Glycemic Control and Hospital Outcomes for Inpatients Treated with Glargine or Detemir Insulin

Glycemic Control	Glargine	Detemir	p-value
Admission HbA1c, % (mean, SD)	8.2 ± 2.1	8.2 ± 1.8	0.60
Admission BG, mg/dL (mean, SD)	184.9 ± 79.0	184.9 ± 73.9	0.47
Mean daily hospital BG, mg/dL (mean, SD)	181.5 ± 46.1	180.3 ± 43.6	0.70
Max BG (first 48 hours), mg/dL (mean, SD)	270.7 ± 89.1	264.3 ± 85.1	0.16
Any BG > 250 mg/dL during hospitalization, n (%)	4048 (70.4)	343 (69.2)	0.56
Hypoglycemic events			
BG < 70 mg/dL, n (%)	1662 (28.9)	166 (33.5)	0.03
BG < 40 mg/dL, n (%)	287 (5)	26 (5.2)	0.80
Nocturnal (midnight to 06:00 AM) (BG < 70 mg/dL), n (%)	579 (10.1)	55 (11.1)	0.47
Insulin therapy (mean, SD)			
Total daily insulin dose, units/kg/d (mean, SD)	0.22 ± 0.15	0.27 ± 0.16	<0.001
# daily basal insulin injections per day, (mean, SD)	1.07 ± 0.20	1.14 ± 0.28	<0.001
Complications (n, %)			
Hospital mortality	70 (1.2)	2 (0.4)	0.12
Composite of complications	2392 (41.6)	208 (41.9)	0.89
- Major adverse cardiac events	900 (15.7)	83 (16.7)	0.53
- Stroke	141 (2.5)	16 (3.2)	0.29
- Acute kidney injury	964 (16.8)	65 (13.1)	0.04
- Acute respiratory failure	142 (2.5)	4 (0.8)	0.01
- Pneumonia	231 (4.0)	6 (1.2)	<0.001
- Bacteremia	108 (1.9)	6 (1.2)	0.38
- Wound infection	55 (1.0)	8 (1.6)	0.16
Hospital-related outcomes			
Hospital LOS, median, days (IQR)	4 (3.0, 8.0)	4 (2.0, 7.0)	0.001
Hospital LOS, mean, days (SD)	6.8 (±7.4)	6.0 (±6.3)	<0.001
Readmissions, n (%)	192 (3.3)	23 (4.6)	0.13

HbA1c (hemoglobin A1c), BG (blood glucose), LOS (length of stay), IQR (interquartile range), eGFR (estimated glomerular filtration rate).

Table 3**Hypoglycemia Risk and Glycemic Control Adjusted for Renal Function**

BG <70 mg/dL		Unadjusted ^a	Adjusted ^b
Glargine exposure, eGFR ≥ 60		Reference	Reference
Glargine exposure, eGFR < 60		1.8 (1.6–2.0)	1.8 (1.5–2.2)
Detemir exposure, eGFR ≥ 60		1.2 (0.9–1.6)	1.1 (0.7–1.8)
Detemir exposure, eGFR < 60		2.3 (1.7–3.0)	2.1 (1.4–3.1)
BG ≥ 70 mg/dL and <180 mg/dL			
Glargine exposure, eGFR ≥ 60		Reference	Reference
Glargine exposure, eGFR < 60		0.8 (0.6–1.1)	0.7 (0.4–1.0)
Detemir exposure, eGFR ≥ 60		0.7 (0.3–1.4)	0.7 (0.2–2.5)
Detemir exposure, eGFR < 60		1.0 (0.5–1.8)	1.4 (0.7–3.1)

Data reported as odds ratio (OR) with 95% confidence interval (CI).

^aCrude model.

^bAdjusted for age, race, gender, body mass index, admission service and admission HbA1c.

Estimated glomerular filtration rate (eGFR) based on Modification of Diet in Renal Disease (MDRD) formula. Data adjusted for age, race, gender, body mass index, admission service and admission HgA1c.