

## Glycemic Control and Clinical Outcomes for Patients Admitted to Noncritical Care Hospital Units

### Introduction

Diabetes mellitus and newly recognized hyperglycemia are common comorbidities for patients admitted to the hospital. A study of 2030 consecutive admissions to Georgia Baptist Medical Center in Atlanta in 1998 found a 26% prevalence of diabetes, and 12% of patients were significantly hyperglycemic but did not have a pre-hospital diagnosis of diabetes. The prevalence of diabetes mellitus among US hospital patients increased 48% from 1991–2001, and the costs of hospital-related care for US diabetic patients exceed the costs of all categories of ambulatory diabetes care combined.<sup>1-3</sup>

The impact of glycemic control on clinical outcomes has been studied extensively in the critical care setting, but little is known about the clinical impacts of diabetes mellitus and glycemic control on noncritical care hospital services. Diabetic patients and patients with newly diagnosed hyperglycemia admitted to noncritical care units in the Georgia Baptist Medical Center study had significantly greater hospital length of stay (LOS) and were more likely to die in the hospital or be discharged to a nursing home than nondiabetic patients. However, the study did not assess the impact of glycemic control on hospital outcomes. This article reviews recent investigations of the impact of glycemic control on outcomes for diabetic patients admitted to noncritical care units, the utility of basal/bolus insulin regimens to control hyperglycemia on noncritical care services, and the hospital admission as an opportunity to improve ambulatory glycemic control.<sup>1</sup>

### Glycemic Control and Clinical Outcomes on Noncritical Care Hospital Services

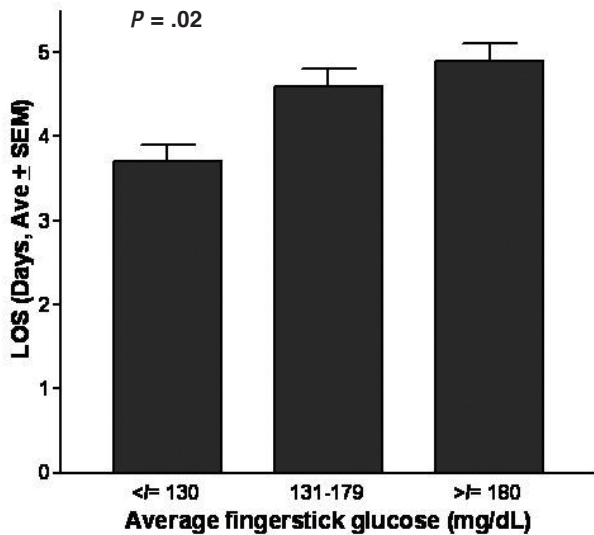
Despite the pervasiveness of diabetes on noncritical care hospital services, little has been published on the relationship between hyperglycemia and clinical outcomes on general hospital units. However, glyce-

mic control clearly has been demonstrated to impact patient outcomes in the Intensive Care Unit (ICU). Insulin infusion therapy to “clamp” blood glucose in a narrow and near physiological range has been demonstrated to reduce mortality and morbidity in the Coronary Care Unit, surgical ICU, and medical ICU.<sup>4-7</sup>

Recent research by our group demonstrates that glycemic control is significantly associated with clinical outcomes of general medicine and family practice hospital services. Glycemic control, assessed as both average finger-stick glucose (FSG) and glycemic variability (standard deviation of FSG), was determined for 898 patients with a primary or secondary diagnosis of diabetes mellitus admitted to the internal medicine and family practice services at Carle Foundation Hospital in 2004. Average FSG values were grouped according to American Diabetes Association (ADA) guidelines for acceptable glycemic control (< 130 mg/dL, 131-179 mg/dL, > 180 mg/dL), and standard deviation (SD) of FSG was grouped into tertiles.<sup>8</sup>

Hospital LOS increased by over a day across categories of average FSG and tertiles of SD of FSG, and nonparametric one-way ANOVA demonstrated that the associations between both average FSG and LOS ( $P = .0005$ ) and glycemic variability and LOS ( $P < .0001$ ) are highly and statistically significant. (Figures 1 and 2) After controlling for factors that effect hospital outcomes, including age, Charlson Comorbidity Index (a weighted measure of prognostically significant comorbid conditions that influence clinical outcomes such as mortality), Apache II score (a measure of illness severity at hospital admission) modified for noncritical care patients, and outpatient mode of diabetes therapy, the associations between average FSG and LOS ( $P = .02$ ) and glycemic variability and LOS ( $P = .007$ ) remained significant in multivariate regression analyses.<sup>8-10</sup>

**Figure 1.**

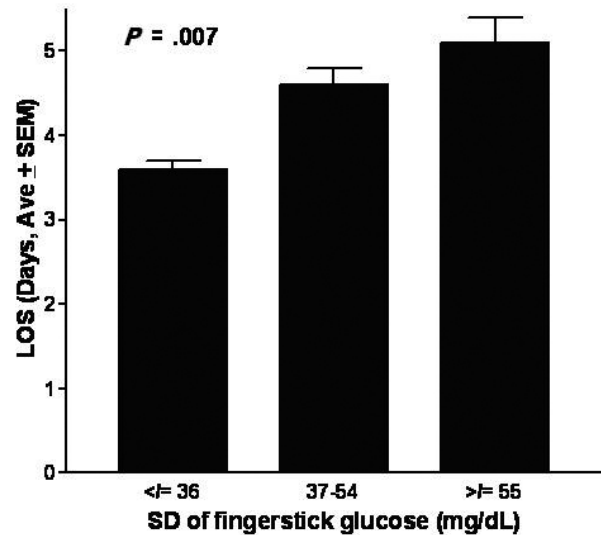


Average FSG levels and glycemic variability are also significantly associated with patient disposition at hospital discharge. Patient places of origin were determined, and discharge outcomes were grouped into four categories: home to home, home to extended care facility (ECF), ECF to ECF, or death in the hospital. When controlled for age, CCI, APACHE II score and hospital diabetes regimen, average FSG values ( $P = .0167$ ) and glycemic variability ( $P = .0173$ ) were shown to correlate significantly with discharge disposition.<sup>8</sup>

### Basal/Bolus Insulin Improves Glycemic Control and Clinical Outcomes

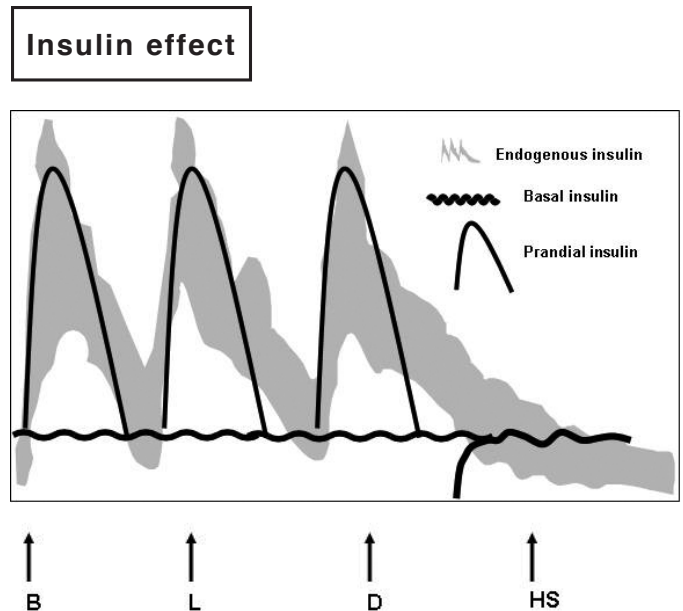
Despite studies demonstrating its limitations, “sliding scale insulin” (SSI) remains the most popular strategy for managing diabetes on noncritical care hospital units. A recent study at Carle Foundation Hospital found that approximately 90% of patients admitted to the internal medicine service were managed with SSI alone or in combination with a patient’s home diabetes regimen. On the Johns Hopkins University internal medicine service, 40% of diabetic patients managed with SSI experienced hyperglycemia, defined as an FSG > 300 mg/dL, 25% had multiple FSG measurements exceeding 300 mg/dL, and 23% experienced at least one episode of hypoglycemia (FSG < 60 mg/dL). A University of Colorado study found that SSI returned FSG to the premeal range of 90–130 mg/dL in only 12% of over 600 FSG measurements. Finally, there were no differences in glycemic control or clinical outcomes for diabetic patients admitted to the family practice service at the Medical University of South Carolina and managed with either SSI alone or SSI in combination with home diabetes medications.<sup>11-14</sup>

**Figure 2.**



The introduction of rapid-acting insulin analogs such as insulin lispro (Humalog) and long-acting insulin analogs such as insulin glargine (Lantus) or insulin detemir (Levemir) permits the use of basal/bolus insulin regimens that mimic endogenous insulin release by a non-diabetic pancreas. (Figure 3) The pharmacokinetic properties of insulin analogs allow greater ease and flexibility in titrating doses to the desired glycemic effect and in principle should result in better glycemic control than prevalent modes of hospital diabetes management.

**Figure 3.**



Recent studies demonstrate that basal/bolus insulin is superior to conventional management of diabetes on general hospital services. In 2005, a group of diabetic patients (N = 116) admitted to the internal medicine service at Carle Foundation Hospital were managed with a basal/bolus insulin regimen utilizing insulin glargine (Lantus) as basal insulin and insulin aspart (Novolog) as prandial insulin. All ambulatory diabetes medications were stopped. Average FSG fell by over 40 mg/dL in the first 24 hours after admission for protocol-managed patients, a highly and statistically significant improvement (P = .0002) that persisted to hospital discharge (P = .0009). (Table 1) There was no improvement in glycemic control among a cohort of historical control patients (N = 176) admitted to the internal medicine service at Carle Foundation Hospital during a similar period in 2004 and managed mostly with SSI and patients' home diabetes regimens. Hypoglycemia occurred more often in the basal/bolus insulin protocol group compared to historical controls (4.5% vs 2.2%) but was still quite infrequent. The six month results of a recently completed Carle Foundation Hospital diabetes team study also demonstrate the superiority of basal/bolus insulin to prevalent diabetes management practices. Average FSG improved by 30–50 mg/dL from baseline after the diabetes team assumed responsibility for diabetes care and implemented basal/bolus insulin management.<sup>8-11</sup> (Table 2)

**Table 1. Glycemic Control for Basal/Bolus Insulin Protocol Patients and Historical Control Patients in the Carle Foundation Hospital Basal/Bolus Insulin Study (Finger-stick Glucose, Mean ± SD, mg/dL)**

	Admissions	24 Hour	Discharge
Protocol	197 ± 104 <sup>a,b,c</sup>	154 ± 67 <sup>b</sup>	159 ± 62 <sup>c</sup>
Control	166 ± 68 <sup>a</sup>	159 ± 61	166 ± 69

- <sup>a</sup> P = .0051 for comparison of admission finger-stick glucose between groups
- <sup>b</sup> P = .0002 for comparison of 24-hour protocol finger-stick glucose to admission
- <sup>c</sup> P = .0009 for comparison of protocol discharge finger-stick glucose to admission

All other comparisons NS

**Table 2. Glycemic Control for Patients on the General Medicine and Surgery Services at Carle Foundation Hospital Before and After Management by the Hospital Diabetes Care Team**

	N	Before Consult	After Consult	P Value
All	268	199 ± 67	159 ± 38	< .0001
Surgery	68	185 ± 56	153 ± 35	.0001
Medicine	132	210 ± 72	163 ± 38	< .0001

Average ± SD of finger-stick glucose, comparison by t-test with Welch correction

Other groups have recently published findings similar to our results. Diabetic patients (N = 130) admitted to the general medicine services at Grady Hospital in Atlanta, Georgia and Jackson Memorial Hospital in Miami, Florida were randomized to management with SSI or a basal/bolus insulin regimen utilizing insulin glargine and insulin glulisine (Apidra). The average FSG curves began to separate in favor of basal/bolus insulin 24 hours after admission, and the difference in average FSG between the two groups was statistically significant in favor of basal/bolus insulin by the fourth hospital day. The Northwestern University Glucose Management Service implemented a basal/bolus insulin protocol on the general surgery service and documented an approximately 20 mg/dL improvement in average FSG compared to historical controls that was statistically significant.<sup>15-16</sup>

Our 2005 study of basal/bolus insulin on general medicine appears to be the only one that measured clinical endpoints. Compared to historical controls, hospital LOS was nearly one day shorter for insulin protocol managed patients (4.5 vs 3.6 days, P = .02). (Table 3) Hospital charges in 2005 dollars were approximately \$1700 less for insulin protocol treated patients, though this difference was not statistically significant given the relatively small size of the study. Hospital disposition, the likelihood of discharge to home or an extended care facility, was no different between the two groups. Multiple studies now demonstrate that basal/bolus insulin therapy clearly controls hyperglycemia better than typical approaches at diabetes management on general hospital services, and our group's study at Carle Foundation Hospital found that a basal/bolus insulin regimen also shortened hospital LOS.<sup>11</sup>

**Table 3. Clinical Outcomes for Basal/Bolus Insulin Protocol Patients and Historical Controls in the Carle Foundation Hospital Basal/Bolus Insulin Study**

	Protocol	Control	P
Length of Stay	3.6 ± 3.0	4.5 ± 3.4	.02
Disposition (%)			
Home	68	75	.23
Extended Care	29	24	.34
Deceased	2	1	.65
Transfer	1	—	—
Hospital Charges			
(2005 dollars)	13,901 ± 18,323	15,561 ± 19,183	.46

### Hospital Admission as an Opportunity to Improve Ambulatory Glycemic Control

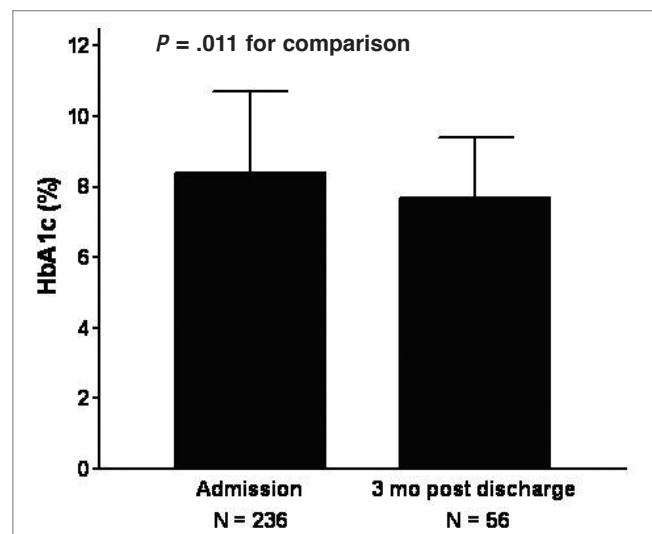
Many diabetic patients are under suboptimal glycemic control at time of hospital admission. In the Carle Foundation Hospital basal/bolus insulin study, average HbA1c in the insulin protocol group was 7.8% and 35% of patients had an HbA1c equal to or greater than 8% within three months of admission. Average HbA1c for patients admitted to the Carle Foundation Hospital general medicine or family practice services in 2004 and included in our study of the relationships between glycemic control and clinical outcomes was 7.4%, with 27% of patients presenting with HbA1c equal to or greater than 8%. Finally, patients managed by the Carle Foundation Hospital diabetes team in the first six months of the study had an average HbA1c of 8.4%, and 49% of these patients had a HbA1c of equal to or greater than 8%.<sup>8</sup>

Though many diabetic patients are admitted to the hospital with failed ambulatory treatment regimens, these regimens are often continued without modification when patients are discharged home. In the Carle Foundation Hospital 2004 general medicine and family practice cohort, over half of patients (84/154, 54.5%) with HbA1c of equal to or greater than 8% at time of admission were discharged on their failed home diabetes regimen without any modifications. This may be in part due to perception that patients are unwilling to change diabetes treatment or start insulin while in the hospital. However, a study of elderly patients (N = 57, average age 70 years) admitted to the hospital on oral diabetes medications and in poor glycemic control (average HbA1c 9.7%) found equal acceptance for continuation of oral medications, changing to a twice daily regimen of NPH insulin, or changing to

basal/bolus insulin therapy. In the outpatient follow-up of the Diabetes and Insulin-Glucose Infusion in Acute MI Study (DIGAMI), 86% of patients in the intensive treatment arm were discharged on four shots of insulin per day, and 72% were still compliant with their insulin regimen a year later. Available studies of hospitalized diabetic patients with poor glycemic control demonstrate that they are willing to change their treatment regimen and take insulin if necessary.<sup>17,18</sup>

One of the prespecified endpoints of the Carle Foundation Hospital diabetes care team study was to determine the potential for implementing ambulatory basal/bolus insulin regimens for patients with suboptimal glycemic control prior to hospital admission. A significant majority of patients (80%) agreed to a discharge basal/bolus regimen of insulins aspart and glargine compared to only 50% who were managed with any type of insulin regimen at time of hospital admission ( $P < .0001$ ). Average HbA1c for the entire group of diabetes team patients for whom measurements were available three months after hospital discharge (N = 56) improved by 0.7% from admission ( $P = .011$ ). (Figure 4) Paired measurements at hospital admission and three months after discharge were available for 39 patients; HbA1c improved for 32 patients (82%), and the average HbA1c decrease for paired data points was 1.2%. Only a small number of patients discharged on basal/bolus insulin (23, 11.5%) stopped their regimen three months after hospital discharge.<sup>8</sup>

**Figure 4.**



Just as basal/bolus insulin was demonstrated to benefit patients with Type 1 diabetes in the Diabetes Control and Complications Trial, basal/bolus insulin provides significant clinical benefit for patients with Type 2 diabetes. In the DIGAMI study, mortality in the inten-

sive insulin treatment arm (insulin infusion followed by four shots a day of insulin in the ambulatory setting) was reduced 28% compared to the control group. The Kumamoto University study randomized 110 Japanese men with Type 2 diabetes in equal numbers to therapy with NPH insulin twice a day or regular insulin with meals and NPH insulin at bedtime. At ten year follow-up, the risk of microvascular complications (eg, retinopathy, microalbuminuria) was reduced by 60–100% in the four doses of insulin per day treatment group, and mortality in the multiple daily injection group was 80% lower than in the NPH insulin only group.<sup>18-20</sup>

## Summary

Diabetes mellitus and previously unrecognized hyperglycemia affect nearly 40% of patients on noncritical care hospital units. Glycemic control has a significant impact on outcomes for patients on noncritical care units just as it does for patients in the ICU. Basal/bolus insulin regimens are clearly superior to prevalent methods of diabetes management on general hospital services in controlling hyperglycemia, and there is some evidence that improved glycemic controls helps to shorten hospital LOS. Patients with failed ambulatory treatment regimens are receptive to making therapeutic changes during hospitalization, and initiation of basal/bolus insulin in the hospital has been found to have good acceptance in the outpatient setting and to significantly improve outpatient glycemic control.

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