Reduction of Surgical Mortality and Morbidity in Diabetic Patients Undergoing Cardiac Surgery With a Combined Intravenous and Subcutaneous Insulin Glucose Management Strategy

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OBJECTIVE — To determine if glucose management in postcardiothoracic surgery patients with a combined intravenous (IV) and subcutaneous (SC) insulin regimen reduces mortality and morbidity in patients with diabetes and stress-induced hyperglycemia.

RESEARCH DESIGN AND METHODS — Retrospective review of 614 consecutive patients who underwent cardiothoracic (CT) surgery in 2005 was performed to evaluate the incidence and treatment of postoperative hyperglycemia and operative morbidity and mortality. Hyperglycemic patients (glucose >6.05 mmol/l) were treated with IV insulin in the intensive care unit (ICU) followed by SC insulin (outside ICU). Subgroup analysis was performed on 159 coronary artery bypass grafting (CABG)-only patients.

RESULTS — Among all CT surgeries, patients with a preoperative diagnosis of diabetes had higher rates of postoperative mortality (7.3 vs. 3.3%; $P = 0.03$) and pulmonary complications (19.5 vs. 11.6%; $P = 0.02$) but had similar rates of infections and cardiac, renal, and neurological complications on univariate analysis. However, on multivariate analysis, a preoperative diagnosis of diabetes was not a significant factor in postoperative mortality or pulmonary complications. In CABG-only patients, no significant differences were seen in outcomes between diabetic and nondiabetic patients. Independent of diabetic status, glucose ≥11 mmol/l on ICU admission was predictive of higher rates of mortality and renal, pulmonary, and cardiac postoperative complications.

CONCLUSIONS — A combination of IV insulin (in the ICU) and SC insulin (outside the ICU), a less costly and less nursing-intensive therapy than 3 days of IV insulin postoperatively, results in a reduction of the increased surgical morbidity and mortality in diabetic patients after CT surgery.

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Abbreviations: CABG, coronary artery bypass grafting; CT, cardiothoracic; ICU, intensive care unit; IV, intravenous; SC, subcutaneous.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

The leading cause of death among individuals with diabetes is cardiovascular disease, and the prevalence of diabetes among patients undergoing coronary artery bypass grafting (CABG) has been reported as high as 34% (1). Historically, diabetic patients have had worse surgical outcomes when compared with individuals without diabetes, specifically higher perioperative mortality (2), deep sternal wound infections (3), postoperative strokes, and longer length of hospital stays (4). Surgical outcomes have been associated with the presence and degree of hyperglycemia in the postoperative period independent of a prior diagnosis of diabetes (5).

After cardiac surgery, most patients are sent to the intensive care unit (ICU), and even a modest degree of hyperglycemia occurring after ICU admission is associated with a substantial increase in hospital mortality (5). Glucose control via continuous intravenous (IV) insulin infusions for 3 days postoperatively has been shown to eliminate the incremental increase in in-hospital mortality and deep sternal wound infection rates after CABG associated with diabetes (3,6).

Practically, however, continuous insulin infusions are extremely labor-intensive and costly, so it would be ideal to determine whether similar glycemic control using a subcutaneous (SC) insulin protocol can achieve similar benefits. A protocol has been established at Northwestern Memorial Hospital that is designed to achieve normoglycemia (4.4–6.05 mmol/l) using IV insulin for the immediate postoperative period with transition to a SC insulin regimen upon resolution of critical illness, initiation of oral intake, and transfer out of the ICU (7).

The primary objectives of this study were to determine if glucose management in postcardiothoracic surgery patients with a combined IV and SC insulin regimen reduces mortality and morbidity in

Table 1—*Definition of primary and secondary outcomes (from the Society of Thoracic Surgeons database)*

Primary/secondary outcomes	Society of Thoracic Surgeons field definition
Postoperative mortality	Operative mortality including both *1*) all deaths occurring during the hospitalization in which the operation was performed, even if after 30 days, and 2) those deaths occurring after discharge from the hospital, but within 30 days of the procedure, unless the cause of death is clearly unrelated to the operation
Deep sternal wound infection	Deep sternal infection involving muscle, bone, and/or mediastinum requiring operative intervention. Must have I&D, plus wound culture and treatment with antibiotics
Complications/other infections	
Thoracotomy site	Infection involving a thoracotomy or parasternal site. Must have I&D, plus wound culture and treatment with antibiotics
Leg vein harvest site	Infection involving a leg vein harvest site. Must have I&D, plus wound culture and treatment with antibiotics
Sepsis	Postoperative septicemia with positive blood cultures
Complications/neurological	
Permanent deficit	Central neurological deficit persisting postoperatively for >72 h
Transient deficit	Postoperative transient neurological deficit (transient ischemic attack) recovery within 24 h; reversible ischemic neurological deficit recovery within 72 h
Coma	New postoperative coma persisting >24 h secondary to anoxic/ischemic and/or metabolic encephalopathy, thromboembolic event, or cerebral bleed
Complications/pulmonary	
Prolonged ventilation	Pulmonary insufficiency requiring ventilator >24 h postoperatively
Need for reintubation	Patient was reintubated during the hospital stay after the initial extubation
Pulmonary embolism	Pulmonary embolus documented by CT scan, V/Q scan, or angiogram
Pneumonia	Pneumonia diagnosed by positive culture or sputum, transtracheal fluid, bronchial washings, and/or clinical findings consistent with pneumonia, including CXR with pulmonary infiltrates
Complications/renal	Acute or worsening renal failure resulting in either a serum creatinine >2.0 and 2× most recent preoperative creatinine level or a new requirement for dialysis postoperatively
Complications/cardiac	
Perioperative myocardial infarction	Presence of perioperative myocardial infarction documented by CK-MB >5× normal (0–24 h postoperatively) or ST elevation, new Q waves, new LBBB on electrocardiogram, or CK-MB >3× normal (>24 h)
Atrial fibrillation	New onset of atrial fibrillation requiring treatment. Does not include recurrence of atrial fibrillation that had been present preoperatively
Heart block	New heart block requiring implantation of a permanent pacemaker before discharge
Cardiac arrest	Cardiac arrest documented by one of the following: ventricular fibrillation, rapid ventricular tachycardia with hemodynamic instability, asystole
Aortic dissection	Dissection along any part of the aorta
Readmission within 30 days	Readmission as inpatient within 30 days from the date of initial surgery for *any* reason

CK-MB, creatine kinase–MB; CXR, chest X ray; I&D, incision and drainage; LBBB, left bundle branch block; V/Q, ventilation/perfusion.

diabetic patients and, in those diabetic patients undergoing CABG only, compare surgical outcomes with studies in which patients receive 3 days of continuous IV insulin.

RESEARCH DESIGN AND METHODS

— A retrospective review of 622 consecutive patients who underwent cardiothoracic (CT) surgery between 1 January 2005 and 31 December 2005 at Northwestern Memorial Hospital, a 776-bed tertiary care center in Chicago, Illinois, was performed to evaluate the incidence and treatment of postoperative hyperglycemia and operative morbidity and mortality. Out of 622 patients, 8 cases were excluded: 5 died during the initial procedure, 1 had a sternal wire removed and was not admitted to the hospital postoperatively, 1 had a cardiac laceration with hemopericardium and was not under the primary care of cardiac surgeons postoperatively, and 1 was a duplicate entry into the surgical database. After exclusions, the study population consisted of 614 patients. A predefined subgroup analysis was also performed on 159 consecutive patients who underwent CABG only.

Glucose data were collected from patient medical records. Outcomes data were extracted from the Society of Thoracic Surgeons Adult Cardiac Surgery Database, collected by Northwestern Memorial Hospital CT surgeons. Approval for this study was granted by the Northwestern University Institutional Review Board.

The primary outcome of this study was postoperative mortality, as defined in the Society of Thoracic Surgeons database. Secondary outcomes included the incidence of deep sternal wound infection, other infections, pulmonary complications, cardiac complications, renal complications, neurological complications, and readmission to the hospital within 30 days of the initial procedure (Table 1). If a patient had one or more complication within an outcome category, the category was flagged as a single complication.

Statistical analysis on demographic

Table 2—*Diabetes versus nondiabetes (all CT surgery)*

	Diabetes	No diabetes	*P*
n	123	491	—
Male sex	71 (58)	328 (67)	0.07
Caucasian	74 (60)	362 (74)	0.004
Age (years)	65.6 ± 11.1	62.3 ± 14.1	0.02
BMI (kg/m^2)	30.6 ± 7.7	27.3 ± 5.4	<0.001
Hypertension	85 (69)	254 (52)	<0.001
Dyslipidemia	91 (74)	240 (49)	<0.001
Smoking history	59 (48)	183 (37)	0.04
Chronic renal failure	9 (7)	7 (3)	0.08
Chronic lung disease	17 (14)	38 (8)	0.05
Previous myocardial infarction	40 (33)	67 (14)	<0.001
Previous stroke	17 (14)	24 (5)	0.001
Elective surgery	70 (57)	366 (75)	<0.001
GMS consult	115 (94)	437 (89)	0.18
IV insulin protocol	117 (95)	461 (94)	0.83
SC insulin protocol	116 (94)	434 (88)	0.07
Mean glucose on ICU admission (mmol/l)	9.79 ± 3.24	8.74 ± 2.750	0.003
Mean glucose in ICU (mmol/l)	7.59 ± 1.26	7.15 ± 0.99	<0.001
Mean glucose outside ICU (mmol/l)	7.86 ± 1.43	6.54 ± 0.77	<0.001
Total number of glucose values	9,623	28,003	
Number of glucose values <3.3 mmol/l (%)	164 (1.7)	308 (1.1)	<0.0001

Data are *n*, *n* (%), or means ± SD unless otherwise specified. GMS, glucose management service.

data were performed with one-way ANOVA (with Tukey test on all statistically significant results) using GraphPad InStat version 3.00 for Windows 95 (GraphPad Software, San Diego, CA). A χ^2 test or Fisher's exact test (when sample size was small) was used for univariate analysis to compare the incidence between the groups for the primary and secondary outcomes. Subsequently, multivariate analysis was performed using logistic regression to explore the relationship between statistically significant outcomes and the covariates of interest. The multivariate model included the covariates that were significant at the 0.1 level in the univariate analysis. A stepwise model selection technique was used to build the final model. A *P* value ≤0.05 was considered statistically significant. The statistical analysis was carried out using SAS software, version 9.1 (SAS Institute, Cary, NC).

RESULTS — The study cohort is described with respect to demographic characteristics, cardiac risk profile, and glycemic profile in Table 2, comparing those patients who had a preexisting diagnosis of diabetes (diabetic patients, *n* = 123, 20%) with those that did not (nondiabetic patients, *n* = 491, 80%). Significant differences between the diabetic and nondiabetic patients were fewer Caucasians, a higher average age, and a significantly higher BMI in the diabetic group. Traditional cardiac risk factors were significantly more common in the diabetic cohort, specifically hypertension, dyslipidemia, and previous smoking history. Preoperative comorbid illnesses were also present more commonly in the diabetic cohort (specifically chronic lung disease, renal failure, and history of myocardial infarction). Nonelective cardiac surgery was performed more often in the diabetic cohort. Preoperatively, outpatient antihyperglycemic regimens for the diabetic cohort included insulin (27%), oral hypoglycemic agents (59%), diet only (6%), and no treatment (8%).

Postoperatively, hyperglycemia (glucose level >6.05 mmol/l) was almost universal (98% diabetic vs. 99% nondiabetic patients) in the ICU. Independent of diabetic status, ICU admission glucose ≥11 mmol/l was predictive of higher rates of postoperative mortality (6.1 vs. 2.3%; *P* = 0.04) and renal (10.7 vs. 3.9%; *P* = 0.02), pulmonary (21.4 vs. 11.0%; *P* = 0.02), and cardiac (32.1 vs. 21.8%; *P* = 0.02) complications.

In diabetic compared with nondiabetic patients, significantly higher values were found for the mean glucose upon ICU admission, the overall mean glucose in the ICU, and the overall mean glucose after transfer out of the ICU (Table 2). The IV insulin protocol was initiated on 95% of the diabetic and 94% of the nondiabetic patients, and the SC insulin protocol was subsequently initiated on 94% of the diabetic and 88% of the nondiabetic patients. Among all CT surgeries, diabetic patients had higher rates of postoperative mortality (7.3 vs. 3.3%; *P* = 0.03) and pulmonary complications (19.5 vs. 11.6%; *P* = 0.02) but had similar rates of deep sternal wound infections, other in-

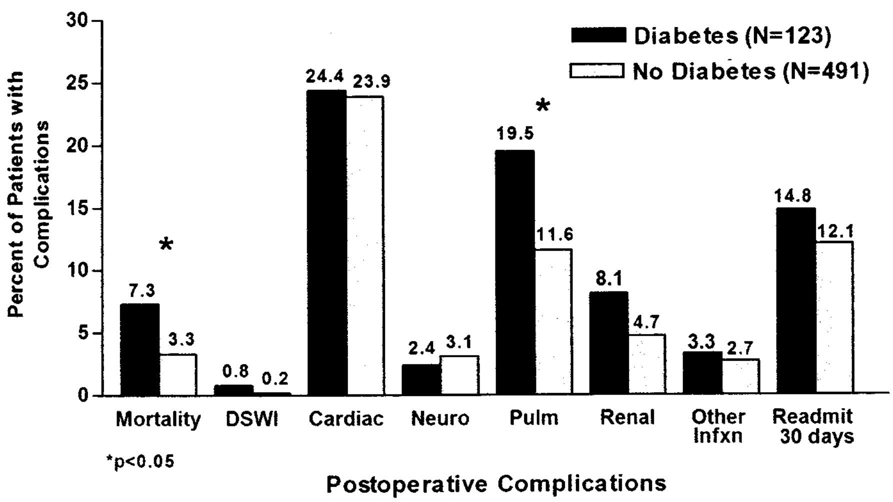

Figure 1—*Postoperative morbidity and mortality in CT surgery patients with and without diabetes. Diabetic patients had higher rates of postoperative mortality (*P *= 0.04) and pulmonary complications (*P *= 0.02) but had similar rates of deep sternal wound infections, other infections, and cardiac, renal, and neurological complications than nondiabetic patients, as shown here on univariate analysis. On multivariate analysis, it was found that the presence of diabetes was not a significant factor in either pulmonary complications or mortality. DSWI, deep sternal wound infections; Infxn, infection; Neuro, neurological complications; Pulm, pulmonary complications.*

Table 3—*Diabetes versus nondiabetes (CABG only)*

	Diabetes	No diabetes	*P*
n	48	111	—
Male sex	34 (71)	89 (80)	0.22
Caucasian	29 (60)	85 (77)	0.054
Age (years)	65.2 ± 11.2	65.0 ± 10.3	0.91
BMI (kg/m^2)	31.7 ± 8.6	28.0 ± 4.8	<0.001
Hypertension	35 (73)	71 (64)	0.36
Dyslipidemia	39 (81)	78 (70)	0.17
Smoking history	19 (40)	58 (52)	0.17
Chronic renal failure	3 (6)	2 (2)	0.16
Chronic lung disease	2 (4)	4 (4)	1.00
Previous myocardial infarction	21 (44)	33 (30)	0.10
Previous stroke	4 (8)	2 (2)	0.07
Elective surgery	28 (58)	73 (66)	0.38
GMS consult	48 (100)	104 (94)	0.10
IV insulin protocol	48 (100)	105 (95)	0.18
SC insulin protocol	48 (100)	104 (94)	0.10
Mean glucose on ICU admission (mmol/l)	9.79 ± 2.64	8.47 ± 2.09	<0.001
Mean glucose in ICU (mmol/l)	7.64 ± 1.15	7.20 ± 1.0	0.02
Mean glucose outside ICU (mmol/l)	8.3 ± 1.7	6.65 ± 0.71	<0.001
Total number of glucose values	2,378	3,889	
Number of glucose values <3.3 mmol/l (%)	29 (1.2)	23 (0.6)	0.012

Data are *n*, *n* (%), or means ± SD unless otherwise specified. GMS, glucose management service.

fections, and cardiac, renal, and neurological complications than nondiabetic patients on univariate analysis (Fig. 1). However, on multivariate analysis, it was found that the presence of diabetes was not a significant factor in either pulmonary complications or mortality. In this multivariate analysis, renal failure, nonelective surgery, and older age were positively associated with pulmonary complications, and renal failure, nonelective surgery, and female sex were positively associated with postoperative mortality independently of the patient's diabetic status.

Subgroup analysis was also performed on patients who underwent CABG surgery (n = 159; 25.9%) without any other simultaneous surgical procedures. The subgroup consisted of 48 diabetic patients (30.2%) and 111 nondiabetic patients (69.8%). Table 3 describes the demographics, cardiac risk profile, and comorbid illnesses of the CABG-only subgroup. Similar to the entire cohort, diabetic patients undergoing CABG surgery had higher rates of hypertension, dyslipidemia, preexisting renal failure, and chronic lung disease. The nondiabetic cohort had a higher percentage of previous smokers.

In the CABG-only subgroup, use of both IV and SC insulin protocols was similar among diabetic and nondiabetic patients. Mean glucose levels on ICU admission, in the ICU, and outside the ICU were higher in diabetic patients (Table 3). In the CABG-only cohort, no statistically significant differences were seen in primary or secondary outcomes between diabetic and nondiabetic patients using univariate analysis (Fig. 2). No postoperative deaths occurred in this cohort, and there was only one deep sternal wound infection.

The major complication of intensive insulin therapy in the perioperative period is hypoglycemia. Out of 37,626 glucose values reviewed in our study, only 465 (1.2%) were <3.3 mmol/l. Rates were higher in individuals with a prior history of diabetes compared with individuals without such a history in the total group (1.7 vs. 1.1%, P < 0.0001) and those undergoing CABG only (1.2 vs. 0.6%, P = 0.012). None of these episodes were considered severe, and none resulted in loss of consciousness or seizure.

CONCLUSIONS— Hyperglycemia has been shown to be an independent risk factor for poor clinical outcomes in multiple patient populations (8–10). Similarly, we found that a glucose level on ICU admission ≥11 mmol/l was predictive of higher rates of mortality and postoperative complications (renal, pulmonary, and cardiac).

Diabetic patients undergoing CT surgery have been shown to have higher rates of mortality and postoperative complications than nondiabetic patients (4,11,12). Our study demonstrates that glucose management with a combined IV and SC insulin regimen eliminates this known increased postoperative morbidity and mortality in patients with preexisting diabetes not only in those undergoing

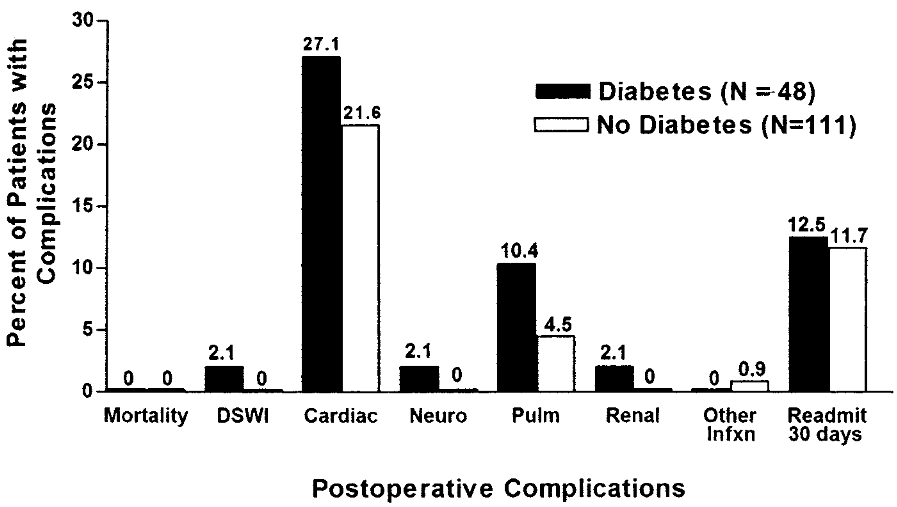

Figure 2—*Postoperative morbidity and mortality in patients undergoing CABG with and without diabetes. There were no statistically significant differences in morbidity and mortality between the groups. DSWI, deep sternal wound infections; Infxn, infection; Neuro, neurological complications; Pulm, pulmonary complications.*

CABG, similar to what has been shown with 3 days of continuous IV insulin infusion (3,6,13,14) but in all CT surgeries. It should be noted that the diabetic patients in our study had postoperative morbidity and mortality rates similar to those without a prior diagnosis of diabetes despite having higher age, BMI, traditional cardiac risk factors (hypertension, dyslipidemia, and smoking history) and more preexisting comorbid illnesses (chronic lung disease, chronic renal insufficiency, previous myocardial infarction, and previous stroke). Although postoperative pulmonary complications and mortality were statistically significant in the diabetic cohort for all cardiac surgery on univariate analysis, they were found to be unrelated to diabetes status on multivariate analysis. The difference in pulmonary complications between diabetic and nondiabetic patients was attributable to higher rates of prolonged ventilation and need for reintubation, and these were positively associated with preexisting renal failure, nonelective surgery, and older age independently of the presence of diabetes. Postoperative mortality was associated with preexisting renal failure, nonelective surgery, and female sex. Mean glucose levels in the immediate postoperative period were slightly higher in the diabetic cohort, but this calculated mean is influenced by the higher mean glucose on ICU admission.

Of those individuals not known to have diabetes, 99% were found to be hyperglycemic postoperatively in our study, with 94% requiring an IV insulin drip for control. Critical illness causes an impairment of insulin secretion and insulin action, resulting in hyperglycemia, even in normal individuals, and a worsening of the hyperglycemia in patients with diabetes (10,13–17). Biochemical studies suggest that mortality is reduced with improved glycemic control due to favorable alterations in myocardial and skeletal muscle metabolism, improved cell membrane stability, myocardial contractility, and endothelial cell function, as well as increased nitric oxide and decreased inflammatory mediators, platelet aggregation, and thrombosis (18–20).

Previously, in a prospective randomized controlled study, Van den Berghe et al. (10) showed that normalization of elevated glucose levels by intensive insulin therapy in patients in the surgical ICU decreased in-hospital mortality by 34%. Post-CABG mortality in diabetic patients undergoing CABG only has been reported to be between 2 and 4% (21–23), but continuous insulin infusion for 72 h postoperatively has been shown to reduce this higher risk (6). In a study of 3,554 diabetic patients undergoing isolated CABG surgery, Furnary et al. (6) reported a mortality rate of 2.5% in patients treated with a 72-h postoperative insulin infusion (mean glucose 9.73 ± 1.65 mmol/l) compared with 5.3% of patients treated with SC insulin therapy (mean glucose 11.71 ± 2.25 mmol/l). Although Furnary et al. did not study the nondiabetic population, they reported an overall CABG mortality rate of 2.8% ($n = 14{,}051$) at their institution. In comparison, in our study of 159 CABG patients, postoperative mortality was nonexistent in both the diabetic and nondiabetic groups.

It is difficult to perform inter-institutional comparison because of differences in surgical experience and techniques. However, we were able to compare our observed mortality results of 0% for both patient groups undergoing CABG surgery with those from the national Society of Thoracic Surgeons 2005 database. According to this database, which adjusts for the various risk factors in our patients, the expected mortality for the group without a prior diagnosis of diabetes was 1.30% (95% CI 0–3.75%), for those with a prior diagnosis of diabetes it was 2.1% (0–8.24%), and for the entire group of 159 patients undergoing CABG it was 1.50% (0–2.65%).

Complications of intensive insulin therapy in our patients were very low. Despite over 90% of patients being treated intensively with insulin therapy, hypoglycemia (glucose <3.3 mmol/l) rates remained low but were higher (1.7 vs. 1.1%, $P < 0.0001$) in individuals with a prior diagnosis of diabetes. None of the hypoglycemic values were deemed severe, and none were associated with loss of consciousness or seizures. Nondiabetic patients were often titrated off SC insulin therapy on postoperative days 4 or 5 because of improvements in postoperative insulin resistance and normalization of blood glucose. The difference in mean glucose levels outside of the ICU can also be explained by the need for continuing to monitor euglycemic nondiabetic patients after cessation of insulin therapy.

There are limitations to our study. Although it was a prospectively designed protocol, it was not a randomized trial comparing different treatment regimens, and there was no control group. We also could not compare surgical complication rates before and after institution of the glycemic protocols because of concomitant changes in the surgeons and changes in a number of aspects of the surgery and perioperative care. Another limitation is the relatively small numbers of patients reported for this single year period. Finally, some of the patients designated as not having diabetes could possibly have had diabetes; it is generally estimated that ~30% of people with diabetes have not been diagnosed (24). Based on the number of patients in our series with diagnosed diabetes, we can estimate that perhaps an additional 54 (11.0%) patients of the "nondiabetic" group for all CT surgery and an additional 15 (13.5%) patients of the "nondiabetic" group undergoing CABG may actually have had diabetes.

In conclusion, in this study, diabetic patients had similar rates of postoperative mortality, deep sternal wound infections, other infections, and pulmonary, cardiac, renal, and neurological complications compared with nondiabetic patients after CT surgery. Thus, for the first time, we have shown that a combination of IV insulin (in the ICU) and SC insulin (outside the ICU), a less costly and less nursing-intensive therapy than 3 days of IV insulin postoperatively, results in a reduction of the increased surgical morbidity and mortality in diabetic patients after CT surgery that has been previously described in the literature.

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References

1. Lauruschkat AH, Arnrich B, Albert AA, Walter JA, Amann B, Rosendahl UP, Alex-

ander T, Ennker J: Prevalence and risks of undiagnosed diabetes mellitus in patients undergoing coronary artery bypass grafting. *Circulation* 112:2397–2402, 2005
2. Weintraub WS, Wenger NK, Jones EL, Craver JM, Guyton RA: Changing clinical characteristics of coronary surgery patients: differences between men and women. *Circulation* 88:78–86, 1993
3. Furnary AP, Zerr KJ, Grunkemeier GL, Starr A: Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients after cardiac surgical procedures. *Ann Thorac Surg* 67:352–360, 1999
4. Thourani VH, Weintraub WS, Stein B, Gebhart SSP, Craver JM, Jones EL, Guyton RA: Influence of diabetes mellitus on early and late outcome after coronary artery bypass grafting. *Ann Thorac Surg* 67: 1045–1052, 1999
5. Krinsley JS: Association between hyperglycemia and increased hospital mortality in a heterogeneous population of critically ill patients. *Mayo Clin Proc* 78:1471–1478, 2003
6. Furnary AP, Gao G, Grunkemeier GL, Wu Y, Zerr KJ, Bookin SO, Floten HS, Starr A: Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 125:1007–1021, 2003
7. Desantis AJ, Schmeltz LR, Schmidt K, Mahler E, Rhee C, Wells A, Brandt S, Peterson S, Molitch ME: Inpatient management of hyperglycemia: the Northwestern Experience. *Endocr Pract* 12:491–505, 2006
8. Umpierrez GE, Isaacs SD, Barzagan N, You X, Thaler LM, Kitabchi AE: Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab* 87:978–982, 2002
9. Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC: Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. *Stroke* 32:2426–2432, 2001
10. Van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, Vlasselaers D, Ferdinande P, Lauwers P, Bouillon R: Intensive insulin therapy in the critically ill patients. *N Engl J Med* 345: 1359–1367, 2001
11. Carson JL, Scholz PM, Chen AY, Peterson ED, Gold J, Schneider SH: Diabetes mellitus increases short-term mortality and morbidity in patients undergoing coronary artery bypass graft surgery. *J Am Coll Cardiol* 40:418–423, 2002
12. Herlitz J, Wognsen G, Emanuelsson H, Haglid M, Karlson BW, Karlsson T, Albertsson P, Westberg S: Mortality and morbidity in diabetic and nondiabetic patients during a 2-year period after coronary artery bypass grafting. *Diabetes Care* 19:698–703, 1996
13. Furnary AP, Zerr KJ, Grunkemeier GL, Heller AC: Hyperglycemia: a predictor of mortality following CABG in diabetics. *Circulation* 100:I-591, 1999
14. Zerr KJ, Furnary AP, Grunkemeier GL, Bookin S, Kanhere V, Starr A: Glucose control lowers the risk of wound infection in diabetics after open heart operations. *Ann Thorac Surg* 63:356–361, 1997
15. Hollingdal M, Juhl CB, Dall R, Sturis J, Veldhuis JD, Schmitz O, Porksen N: Glucocorticoid induced insulin resistance impairs basal but not glucose entrained high-frequency insulin pulsatility in humans. *Diabetologia* 45:49–55, 2002
16. Pittas AG, Siegel RD, Lau J: Insulin therapy for critically ill hospitalized patients: a meta-analysis of randomized controlled trials. *Arch Intern Med* 164:2005–2011, 2004
17. Pomposelli JJ, Baxter JK 3rd, Babineau TJ, Pomfret EA, Driscoll DF, Forse RA, Bistrian BR: Early postoperative glucose control predicts nosocomial infection rate in diabetic patients. *J Parenter Enteral Nutr* 22:77–81, 1998
18. Ferrannini E, Santoro D, Bonadonna R, Natali A, Parodi O, Camici PG: Metabolic and hemodynamic effects of insulin on human hearts. *Am J Physiol* 264:E308–E315, 1993
19. Oliver MF, Opie LH: Effects of glucose and fatty acids on myocardial ischaemia and arrhythmias. *Lancet* 343:155–158, 1994
20. Knuuti MJ, Maki M, Yki-Jarvinen H, Voipio-Pulkki LM, Harkonen R, Haaparanta M, Nuutila P: The effect of insulin and FFA on myocardial glucose uptake. *J Mol Cell Cardiol* 27:1359–1367, 1995
21. Ghali WA, Quan H, Brant R: Coronary artery bypass grafting in Canada: national and provincial mortality trends, 1992–1995. *Can Med Assoc J* 159:25–31, 1998
22. McAlister FA, Amad H, Man J, Tandon P, Bistritz L: Diabetes and coronary artery bypass surgery: an examination of perioperative glycemic control and outcomes. *Diabetes Care* 26:1518–1524, 2003
23. Woods SE, Smith JM, Sohail S, Sarah A, Engle A: The influence of type 2 diabetes mellitus in patients undergoing coronary artery bypass graft surgery: an 8-year prospective cohort study. *Chest* 126:1789–1795, 2004
24. National Diabetes Data Fact Sheet, 2005. Accessed at http:www.diabetes.org