A Randomized Study in Diabetic Patients Undergoing Cardiac Surgery Comparing Computer-Guided Glucose Management With a Standard Sliding Scale Protocol

Leif Saager, MD,* Gordon L. Collins, MD,*† Beth Burnside, BA,* Heidi Tymkew, MHS,*† Lini Zhang, MD,* Eric Jacobsohn, MBChB, MHPE, FRCPC,*† and Michael Avidan, MBBCh, FCA*†

Objective: **The aim of this study was to compare a standard insulin protocol with a computer-guided glucose management system to determine which method achieves tighter glucose control.**

Design: **A prospective, randomized trial.**

Setting: **A cardiothoracic intensive care unit (ICU) in a large academic medical center.**

Participants: **Forty patients with diabetes mellitus who were scheduled for cardiac surgery.**

Interventions: **After induction of anesthesia and for the first 9 hours in the ICU, each subject received a standardized infusion of a 10% glucose solution at a rate of 1.0 mL/kg/h (ideal body weight). The subjects were then randomized to have their glucose controlled by either a paper-based insulin protocol or by a computer-guided glucose management system (CG). The desired range for blood glucose was set between 90 and 150 mg/dL.**

Measurements and Main Results: **There were no differences between groups in baseline characteristics. Patients in the CG group spent more time in the desired range during both the intraoperative phase (49% *v* 27%, $p = 0.001$) and the ICU phase (84% *v* 60%, $p < 0.0001$). There were no statistical differences between groups in the number of hypoglycemia episodes.**

Conclusions: **The computer-guided glucose management system achieved tighter blood glucose control than a standard paper-based protocol in diabetic patients undergoing cardiac surgery. However, the low proportion of blood glucose recordings within the desired range in both groups during the intraoperative period reflects the challenges associated with achieving normoglycemia during cardiac surgery.**

KEY WORDS: hyperglycemia, tight glucose control, computer-guided insulin protocol

PATIENTS WHO HAVE diabetes mellitus have increased morbidity and mortality after cardiac surgery.[1-3] The DIGAMI study suggested that if blood glucose is tightly controlled, patients with diabetes have improved outcome after myocardial infarction.[4] Similarly, evidence has emerged in the surgical, anesthesia, and critical care literature that patients with diabetes have improved outcomes when the blood sugar is well controlled.[5] Even in patients without diabetes, the provision of glucose, insulin, and potassium (GIK) has been associated with improved outcome after myocardial infarction and after cardiac surgery.[6-8] The provision of usable energy substrates to the heart in the form of the insulin-glucose combination may have additive benefit over the control of blood sugar alone.[9-12] Increasing evidence is emerging that the combined strategy of the GIK infusion with tight blood sugar control in patients undergoing cardiac surgery is associated with improved outcomes. The evidence is the strongest for patients who have diabetes. Studies have shown a lower incidence of atrial fibrillation, inotrope requirements, need for pacing, intensive care unit (ICU) stay, recurrent myocardial ischemia, renal failure, wound infection, and postoperative death.[5] Even very brief elevations in blood sugar may be associated with complications, such as wound infections.[13]

One of the major problems associated with the GIK regimens is the observation that during surgical stress there has been a trend toward hyperglycemia.[14] Several intravenous insulin protocols have been developed for trying to achieve tight blood sugar control. One such protocol targeting blood sugar concentrations between 90 and 150 mg/dL currently guides the standard of care in the surgical and cardiothoracic ICUs at the authors' institution. However, because of the implementation of this insulin protocol, patients continue to have episodes of high and low blood sugar, which is likely to be exacerbated by the administration of a GIK solution containing high concentrations of both glucose and insulin. The main limitation with some insulin protocols is that the adjustments to insulin dosage are based only on single blood sugar readings. There is no attempt to incorporate a trend of blood sugar results, which when mathematically modeled can determine a patient's insulin resistance and theoretically control blood glucose more tightly. This approach would theoretically facilitate more accurate insulin administration and decreased overshooting in both directions.

Computer-guided glucose management systems are specifically designed with mathematical modeling to tailor the insulin dosing to the individual patient with frequently changing requirements. Trends of glucose readings are analyzed and modeled to formulate a patient-specific insulin-resistance curve. Adjustments are made in the dosing curves according to predictive mathematical models to prevent episodes of hypoglycemia and hyperglycemia. The ability to perform complex mathematical analysis of past blood glucose readings to determine slopes and standard deviation from slopes is beyond the training of most nurses and physicians in the operating room and ICU. Therefore, the concept of designing a computer program to model glycemic control makes sense when considering the complex relationships that are occurring when patients are under surgical stress.

Diabetic patients undergoing cardiac surgery have rapidly changing and unpredictable insulin requirements in the perioperative period. Because computer-guided systems are specifi-

*From the Departments of *Anesthesiology and †Surgery, Washington University School of Medicine, St Louis, MO.*

Supported by a Barnes-Jewish Hospital Innovation grant.

Address reprint requests to Michael Avidan, MBBCh, FCA, Department of Anesthesiology, Washington University School of Medicine, 660 S Euclid Ave, Campus Box 8054, St Louis, MO 63110. E-mail: avidanm@msnotes.wustl.edu

1053-0770/08/2203-0006$34.00/0
doi:10.1053/j.jvca.2007.09.013

cally designed to tailor the insulin dosing to the individual patient who has frequently changing requirements these products may be an effective method of obtaining good glucose control during and after surgery. The purpose of this study was to determine whether tighter blood sugar control was achieved with the current standard ICU paper-based protocol or a computer-guided algorithm.

METHODS

Forty patients with known diabetes (type 1 or 2) who were scheduled for elective cardiac surgery that requires cardiopulmonary bypass were enrolled in this study. There were 24 men and 16 women between the ages of 50 to 85 who took part in this prospective, randomized study. Exclusion criteria included <18 years of age and known pregnancy.

The study protocol was approved by the Human Research Protection Office, and all patients gave written informed consent before study enrollment. Once consent was obtained, the subjects were randomized into 1 of 2 groups. One group (PB) consisted of subjects who had their blood glucose controlled by the standard paper-based ICU insulin protocol (standard of care). The standard paper-based ICU insulin protocol was developed at this institution with the goal of targeting blood sugar concentrations between 90 and 150 mg/dL (see Appendix). This protocol uses a systematic method of giving insulin for specific blood sugars based on the most recent glucose reading. The computer-guided group (CG) was the second study group, and it consisted of subjects who had their blood glucose managed with the EndoTool (MD Scientific, Charlotte, NC) software. The EndoTool Glucose Management System (MD Scientific) is proprietary, patent-pending software. The EndoTool system recommends the insulin dose, glucose determination frequency, and a 50% dextrose dose (when appropriate) for hypoglycemia. This software upregulates and downregulates a quadratic insulin dosing relationship based on the entered blood glucose readings from a point-of-care device. It uses engineering control math that considers the previous 4 dose responses to regulate the dosing relationship. It is designed to be used by trained health care professionals to calculate individual patients' optimal intravenous insulin dose to control blood glucose levels in critically ill patients.

After the induction of anesthesia, each subject received a standardized infusion of a 10% glucose solution at a rate of 1.0 mL/kg/h (IBW). This infusion continued throughout the surgery and was discontinued once the subject had been in the ICU for 9 hours. Blood glucose and potassium concentrations were measured at least hourly while the glucose infusion was running, and insulin (and glucose) administered given according to either the standard-of-care paper-based protocol or the computer-guided recommendations that were calculated by the software. During surgery, the desired blood glucose range was 90 to 150 mg/dL. Intravenous potassium was supplemented on an hourly basis to maintain a blood potassium concentration between 4 and 5.5 mmol/L. This is similar to the GIK regimen that has been shown to be beneficial for diabetic patients undergoing cardiac surgery.[5]

Once the subject had been in the ICU for 9 hours, then the 10% glucose solution was discontinued and the subject's insulin requirements were managed via the standard-of-care method until they were discharged home. The desired blood glucose in the ICU during this time frame was 90 to 150 mg/dL.

All patients had arterial blood drawn from an arterial catheter that was available for routine monitoring procedures for measurement of blood glucose. Whole-blood glucose was analyzed by a SureStep Flexx point-of-care testing device (Lifescan Inc, Milpitas, CA) at all time points of the study. Peripheral arterial blood samples (troponin I, ketones, and brain natriuretic peptide) were collected for analysis before induction of anesthesia, after removal of the aortic cross-clamp and 6 and 12 hours after cardiopulmonary bypass. Triglycerides and HbA1C were obtained before the induction of anesthesia.

Based on a reduction in mean blood glucose that the authors considered clinically significant (30 mg/dL), a power analysis was calculated. To detect a mean decrease of 30 mg/dL (standard deviation = 30 mg/dL) in blood glucose (eg, from 150 to 120 mg/dL), 20 patients in each group (standard protocol and computer-guided protocol) would give a power of 87% with a 2-tailed p value of 0.05. Hypoglycemia was defined as any glucose reading below 60 mg/dL. Normal distribution was tested by using Kolmogorov-Smirnov tests. Continuous variables were compared by using a Student t test (2-sided) or Mann-Whitney U test if appropriate. Categoric variables were assessed via chi-square tests and Fisher exact tests. Repeated measures on continuous dependent variables were analyzed by using repeated-measures analysis of variance for the factor time and group as a between factor. Time within the desired range for cardiac surgery patients was calculated.[15] The authors considered a result statistically significant if probability values were <0.05. All analysis was performed by using SPSS (SPSS Inc, Chicago, IL) version 14 software.

RESULTS

Each study group consisted of 20 patients. The group characteristics are summarized in Table 1. These 2 groups had similar baseline characteristics. There were no differences in the length of surgery (281 ± 82 minutes [PB] v 290 ± 67 minutes [CG], $p = 0.69$), length of cross-clamp (77 ± 29 minutes [PB] v 85 ± 34 minutes [CG], $p = 0.44$) or cardiopulmonary bypass times (123 ± 43 minutes [PB] v 135 ± 33 minutes [CG], $p = 0.36$). The data did not reveal differences in the median ICU length of stay (2.5 days [interquartile range (IQR), 2-4.75] PB v 2.5 days [IQR, 2-6] CG, $p = 0.825$) or hospital length of stay (7.0 days [IQR, 6-11.75] PB v 9.5 days

Table 1. Subject Characteristics

	PB Group (n = 20)	CG Group (n = 20)	p Value
Age (y)	63.6 ± 8.5	69.0 ± 9.4	0.07
Male (n)	12	12	1.00
BMI	33 ± 8	32 ± 8	0.52
Hypertension (n)	20	18	0.49
Chronic heart failure (n)	10	6	0.33
Myocardial infarction (n)	9	9	1.00
Chronic renal failure (n)	1	2	1.00
Ejection fraction (%)	50.8 ± 12.7	48.7 ± 15.2	0.66
Diabetic control			
Diet (n)	2	3	0.58
Oral insulin (n)	10	12	
Sub Q insulin (n)	8	5	
Length of diabetes (y)	9.9 ± 9.1	15.0 ± 14.2	0.21
Preoperative blood glucose (mg/dL)	149 ± 52	128 ± 33	0.14
Preoperative HbA1C (%)	7.0 ± 1.3	6.8 ± 1.5	0.72
Preoperative triglyceride (mg/dL)	152 ± 108	109 ± 47	0.12
Surgical procedure			
CABG (n)	6	11	0.05
Valve replacement (n)	7	4	
CABG + valve replacement (n)	3	0	
Other (n)	4	5	

Abbreviation: CABG, coronary artery bypass graft.

Table 2. Comparison of Glucose Control

	PB Group (n = 20)	CG Group (n = 20)	*p* Value
Operating room			
Number of samples	101	118	0.16
Mean BG (mg/dL)	177 ± 36	147 ± 19	<0.001
BG in range (%)	27	49	<0.001
Time in range (min)	64 ± 85	121 ± 67	0.02
Mean time to			
BG <150 mg/dL (min)	91 ± 121	62 ± 92	0.55
BG <60 mg/dL (n)	0	1	1.00
Intensive care unit			
Number of samples	225	223	0.84
Mean BG (mg/dL)	147 ± 27	126 ± 18	0.01
BG in range (%)	60	84	<0.001
Time in range (min)	377 ± 214	536 ± 135	0.01
Mean time to			
BG <150 mg/dL (min)	171 ± 238	40 ± 97	0.02
BG <60 mg/dL (n)	1	4	0.60

Abbreviation: BG, blood glucose.

[IQR, 6-11.75] CG, $p = 0.183$) between the groups There were also no differences in the number of postoperative complications (arrhythmias, prolonged intubation, infection, stroke, or myocardial infarction) between the groups. Both groups showed comparable blood glucose levels, hemoglobin A1C, and triglycerides at baseline.

Overall, patients in the CG group achieved a blood glucose level within the desired range significantly faster compared with patients in the PB group (Table 2). Glucose management by a computer-guided protocol resulted in a significantly tighter control; these patients spent a higher percentage of time within the desired range during surgery as well as during the following 9 hours in the ICU. Repeated-measures analysis of variance for blood glucose levels during surgery showed a significant effect for time ($p = 0.02$) and group ($p < 0.001$). Over the study period in the ICU, a significant group effect ($p = 0.01$) but no effect for time ($p = 0.48$) was found. There was no significant time-group interaction at any time (odds ratio, $p = 0.14$; intensive care unit, $p = 0.48$). Changes in blood glucose levels during surgery and ICU stay are displayed in Figure 1. There were no significant differences between the groups when troponin I, brain natriuretic peptide, and ketones were measured at baseline, after the removal of the cross-clamp, and at 6 hours and 12 hours after surgery.

In the computer-based protocol, there was 1 episode of hypoglycemia (blood glucose level = 59 mg/dL) during the intraoperative period and 4 episodes of hypoglycemia in the ICU period (blood glucose range, 48-57 mg/dL). There were no occurrences of hypoglycemia during the intraoperative period in the paper-based protocol and only 1 occurrence of hypoglycemia (blood glucose level = 59 mg/dL) during the ICU period.

DISCUSSION

The importance of good glycemic control in hospitalized patients has been well documented in the literature.[4,5,16-19] These studies have shown a decrease in morbidity and mortality when glucose is tightly controlled during a patient's hospitalization. In this study, the authors were not trying to prove that glycemic control is important, that has already been shown. The authors were comparing a standardized ICU protocol that only incorporates changes to insulin dosing based on individual readings with that of a computer-guided system that bases the insulin doses on trends of glucose readings.

The results of this study show that the CG group achieved tighter glycemic control more rapidly than the patients in the

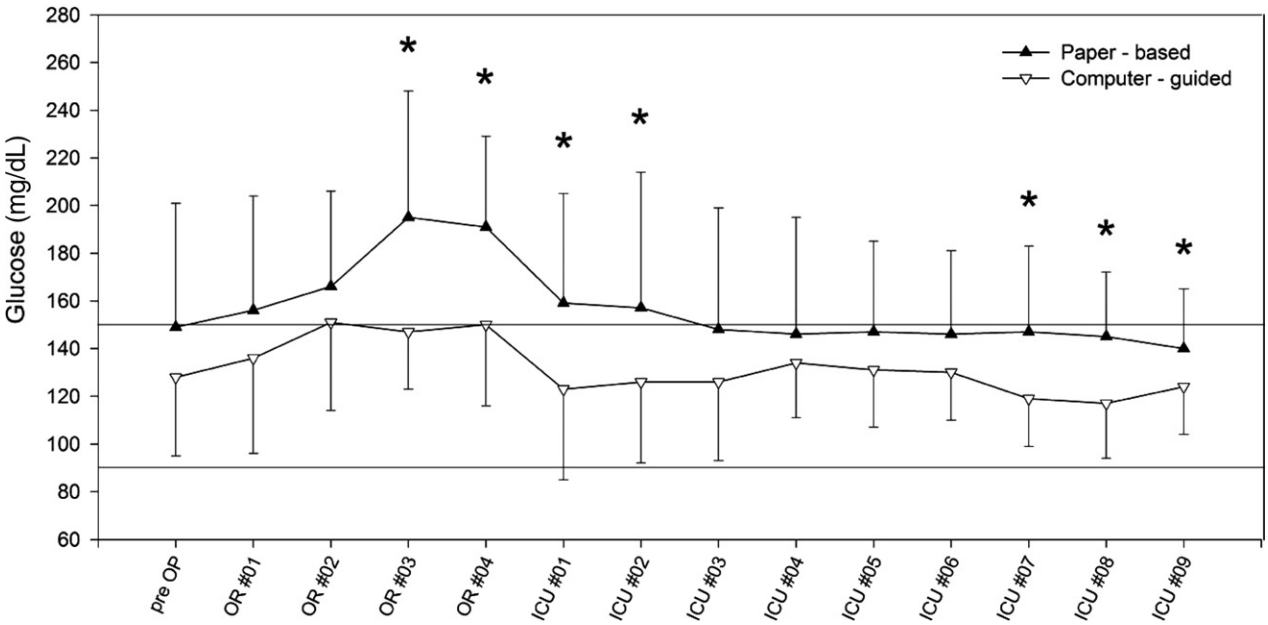

Fig 1. Intra- and postoperative glucose levels. *$p < 0.05$. Pre OP, baseline measurements; OR#1-4, time points in the OR; ICU#1-9, time points in the ICU.

standardized PB group. The Endotool Glucose Management System is a fairly new device that has not been extensively studied. Cochran et al[20] reported the use of this system over an 18-month period in the ICU setting. These authors report that this device provided effective and safe blood glucose control in the ICU population. In addition to the Endotool system, there are other reports of computerized glucose management systems. Boord et al[21] and Vogelzang et al[22] reported that after developing their own computerized insulin protocols glycemic control was improved in the surgical ICU. Plank et al[23] showed that the utilization of an adaptive model predictive control algorithm improved glucose control in patients after cardiac surgery when compared with a standardized insulin protocol. The Glucommander has also been described as a safe, simple, and effective method for maintaining glycemic control in all areas of the hospital, but it has not been compared with a standardized insulin protocol.[24]

There are numerous insulin protocols that have been developed to obtain tight glycemic control. These protocols are often complex and may require tables and sometimes intricate calculations to titrate insulin doses. Also, these protocols may not be sensitive enough for the rapidly changing insulin requirements that are often seen during and after surgery. Because managing glycemia can be challenging during the perioperative period and insulin protocols are often difficult to follow, a computer-guided glucose management system may be helpful in obtaining effective and safe glycemic control. Before deciding what method should be used to achieve glycemic control, consideration should be given to the logistics involved in the successful implementation of this strategy.

Even though the benefits of good glycemic control are well known among health care professionals, implementing such a strategy can often be difficult. Anger and Szumita[25] have described possible barriers of glucose control in the ICU and ways to address those barriers so that glycemic control can be obtained. One of the barriers to the successful implementation of tight glucose control is the increased workload for the nursing staff, which was also apparent in the present study.[26-28] In a study that evaluated the efficiency and safety of a nurse-managed insulin protocol, there was a 35% increase in the number of bedside glucose readings.[26] The increase in bedside glucose readings resulted in an increase in the nursing workload. Aragon[28] estimated that tight glycemic control could result in a major increase in medical costs because of the labor and supplies involved. An additional 2 hours of labor may be required for tight glycemic control for a single patient in a 24-hour period.

Another barrier to glycemic control is the fear of hypoglycemia.[25] Some of the insulin (paper- and computer-guided) protocols require large amounts of insulin to be given when hyperglycemia is still present despite a current insulin infusion. The need for large doses of insulin often impedes the clinician's willingness to comply with tight glucose control out of concern for the patient's safety. This was apparent in this study when larger doses of insulin were recommended by the computer-guided system for treatment of hyperglycemia. The clinicians and nurses were often resistant to administering the recommended insulin dose for fear of hypoglycemia.

Hypoglycemia did occur more frequently in the CG group in the operating room (OR) and the ICU, but it was not statistically significant. The incidence of hypoglycemia in the CG group was 1 of 118 (0.84%) in the OR and 4 of 223 (1.8%) in the ICU compared with the PB group who had 0% incidence in the OR and 1 of 225 (0.44%) in the ICU. Of note, of the 4 occurrences of hypoglycemia in the ICU phase in the CG group, 3 of these episodes occurred within the same patient who was on very low doses of insulin (0-0.5 U/h). Despite the episodes of hypoglycemia in the CG group, these finding are similar to the report published by Cochran et al[20] who had a low incidence of hypoglycemia (blood glucose $<$ 60 mg/dL) of 0.97% in the ICU.

There are several limitations in this study. A uniform population was not enrolled. The authors enrolled any cardiac surgery patient who would require the use of cardiopulmonary bypass. Although the cardiopulmonary bypass time was similar between groups (123 $\pm$ 43 minutes [PB] *v* 135 $\pm$ 33 minutes [CG], $p = 0.36$), the PB group had more combined and valvular surgeries. Another limitation of this study is that the authors only implemented the study intervention for a short period of time (9 hours). The outcome measured in this study was a surrogate outcome (blood glucose control) rather than a clinical outcome. The small number of patients prevented the authors from determining if the computer-guided protocol reduced postoperative complications. A large clinical trial would be required to detect difference in clinical outcomes.

In summary, a computer-guided glucose management system allowed more rapid and tighter glucose control during and immediately after cardiac surgery. However, any method of achieving tight blood sugar control may require increased resources and active participation of all the clinical staff. Whatever method is chosen to obtain tight glycemic control during and after cardiac surgery, it should not only be safe and effective, but it also has to be cost-effective and not lead to staff neglecting other crucial duties and other ill patients.

APPENDIX: PAPER-BASED PROTOCOL

Insulin Infusion Monitoring:

- BG Q1 hour with insulin infusion initiation
- BG Q2 hours with 2 consecutive values in 80-150 mg/dL range
- BG Q4 hours with 4 consecutive values in 80-110 mg/dL range and stable
- BG Q3 hours if patient with any of the following: creatinine level greater than 1.5, receiving HD or CVVHD. Infusion should only be titrated Q3 hours.
- Resume BG Q1 hour if: BG greater than 250 mg/dL, BG less than 70 mg/dL, BG changes by greater than 60 mg/dL, or patient off infusion longer than 24 hours (decrease BG checks as outlined above)

Use only for initial initiation of insulin infusion or if patient has been off infusion longer than 24 hours

130-170 mg/dL	171-220 mg/dL	221-279 mg/dL	280-329 mg/dL	330-379 mg/dL	380-430 mg/dL	greater than 430 mg/dL
No IVP Infusion @ 1 unit/hour	Give 2 units IVP Infusion @ 1 unit/hour	Give 4 units IVP Infusion @ 2 units/hour	Give 6 units IVP Infusion @ 2 units/hour	Give 8 units IVP Infusion @ 2 units/hour	Give 10 units IVP Infusion @ 3 units/hour	Call MD for orders

Insulin Infusion Titration

Blood Glucose (BG)	**If BG decreasing** - infusion changes	**If BG increasing** - infusion changes
less than 60 mg/dL	D/C insulin infusion. Give 25 ml D 50% IVP, Check BG in 15 minutes, if BG remains less than 60 mg/dL, repeat 25 mL D 50% IVP and call HO. When BG greater than 110 mg/dL resume insulin infusion at 50% of previous rate (round down to whole number: previously 5 units/hour → 2.5 units/hour → 2 units/hour)	
60-90 mg/dL	Stop infusion.	Continue to hold infusion
91-110 mg/dL If BG less than 111 mg/dL × 4 and infusion at 1-2 units/hour obtain order to restart SSI regimen	If BG was 90-120, continue same rate. If BG was 121-200, decrease by 2 units/hour or d/c if less than 2 units/hour If BG was greater than 200, decrease by 3 units/hour or d/c if less than 3 units/hour	Maintain at present rate.
111-150 mg/dL	Continue same rate -If BG ↓"d by greater than 40 mg/dL over 2 hours - stop infusion check BG in 1 hour	Increase by or restart at 1 unit/hour.
151-200 mg/dL	Increase by or restart at 1 unit/hour - If BG ↓"d by 40-60 mg/dL over 2 hours - continue same rate, if greater than 60 mg/dL - stop infusion check BG in 1 hour	Increase by or restart at 2 units/hour. Resume BG Q2 hours.
201-250 mg/dL	Increase by or restart at 2 units/hour	Give 4 units insulin IVP then increase infusion by or restart at 2 units/hour. Resume BG Q2 hours.
251-300 mg/dL	Increase by or restart at 2 units/hour	Give 4 units insulin IVP then increase infusion by or restart at 2 units/hour. Resume BG Q1 hour.
301-349 mg/dL	Increase by or restart at 2 units/hour	Give 6 units insulin IVP then increase infusion by or restart at 3 units/hour. Resume BG Q1 hour.
350-400 mg/dL	Increase by or restart at 3 units/hour	Give 6 units insulin IVP then increase infusion by or restart at 3 units/hour. Resume BG Q1 hour.
greater than 400 mg/dL	Call MD	Call MD

REFERENCES

1. Szabó Z, Håkanson E, Svedjeholm R: Early postoperative outcome and medium-term survival in 540 diabetic and 2239 nondiabetic patients undergoing coronary artery bypass grafting. Ann Thorac Surg 74:712-719, 2002

2. Cohen Y, Raz I, Merin G, et al: Comparison of factors associated with 30-day mortality after coronary artery bypass grafting in patients with versus without diabetes mellitus. Am J Cardio 81:7-11, 1998

3. Carson JL, Scholz PM, Chen YA, et al: Diabetes mellitus increases short-term mortality and morbidity in patients undergoing coronary artery bypass graft surgery. J Am Coll Cardiol 40:418-423, 2002

4. Malmberg K, Ryden L, Hamsten A, et al: Effects of insulin treatment on cause-specific one-year mortality and morbidity in diabetic patients with acute myocardial infarction. DIGAMI study group. Diabetes insulin-glucose in acute myocardial infarction. Eur Heart J 17:1337-1344, 1996

5. Lazar HL, Chipkin SR, Fitzgerald CA, et al: Tight glycemic control in diabetic coronary artery bypass graft patients improves perioperative outcomes and decreases recurrent ischemic events. Circulation 109:1497-1502, 2004

6. Diaz R, Paolasso EA, Piegas LS, et al: Metabolic modulation of acute myocardial infarction. The ECLA (Estudios Cardiologicos Latinoamerica) Collaborative Group. Circulation 98:2227-2234, 1998

7. Bothe W, Olschewski M, Beyersdorf F, et al: Glucose-insulin-potassium in cardiac surgery: A meta-analysis. Ann Thorac Surg 78: 1650-1657, 2004

8. Quinn DW, Pagano D, Bonser RS, et al: Improved myocardial protection during coronary artery surgery with glucose-insulin-potassium: A randomized controlled trial. J Thorac Cardiovasc Surg 131: 34-42, 2006

9. Taegtmeyer H, de Villalobos D: Metabolic support for the postischemic heart. Lancet 345:1552-1555, 1995

10. Taegtmeyer H, Goodwin G, Doenst T, et al: Substrate metabolism as a determinant for postischemic functional recovery of the heart. Am J Cardiol 80:3A-10A, 1997 (suppl 1)

11. Eberli FR, Weinberg EO, Grice WN, et al: Protective effect of increased glycolytic substrate against systolic and diastolic dysfunction and increased coronary resistance from prolonged global underperfusion and reperfusion in isolated rabbit hearts perfused with erythrocyte suspensions. Circ Res 68:466-481, 1991

12. Szabó Z, Arnqvist H, Håkanson E, et al: Effects of high-dose glucose-insulin-potassium on myocardial metabolism after coronary surgery in patients with type II diabetes. Clin Sci 101:37-43, 2001

13. Pomposelli JJ, Baxter JK 3rd, Babineau TJ, et al: Early postoperative glucose control predicts nosocomial infection rate in diabetic patients. J Parenter Enteral Nutr 22:77-81, 1998

14. Bruemmer-Smith S, Avidan MS, Harris B, et al: Glucose, insulin and potassium for heart protection during cardiac surgery. Br J Anaesth 88:489-495, 2002

15. Carr JM, Sellke FW, Fey M, et al: Implementing tight glucose control after coronary artery bypass surgery. Ann Thorac Surg 80:902-909, 2005

16. Van den Berghe G, Wouters P, Weekers F, et al: Intensive insulin therapy in critically ill patients. N Engl J Med 345:1359-1367, 2001

17. Van den Berghe G, Willmer A, Hermans G, et al: Intensive insulin therapy in the medical ICU. N Engl J Med 354:449-461, 2006

18. Langley J, Adams G: Insulin-based regimens decrease mortality rates in critically ill patients: A systemic review. Diabetes Metab Res Rev 23:184-192, 2007

19. Furnary AP, Gao G, Grunkemeier GL, et al: Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting. J Thorac Cardiovasc Surg 125:1007-1021, 2003

20. Cochran S, Miller E, Dunn K, et al: Endotool software for tight glucose control for critically ill patients. Crit Care Med 34:A68, 2006 (suppl 2)

21. Boord JB, Sharifi M, Greevy RA, et al: Computer-based insulin infusion protocol improves glycemia control over manual protocol. J Am Med Inform Assoc 14:278-287, 2007

22. Vogelzang M, Zijlstra F, Nijsten MWN: Design and implementation of GRIP: A computerized glucose control system at a surgical intensive care unit. BMC Med Inform Decis Mak 5:38, 2005

23. Plank J, Blaha J, Cordingley J, et al: Multicentric, randomized, controlled trial to evaluate blood glucose control by the model predictive control algorithm versus routine glucose management protocols in intensive care unit patients. Diabetes Care 29:271-276, 2006

24. Davidson PC, Steed RD, Bode BW: A computer-directed intravenous insulin system shown to be safe, simple, and effective in 120,618 hours of operation. Diabetes Care 28:2418-2423, 2005

25. Anger KE, Szumita PM: Barriers to glucose control in the intensive care unit. Pharmacotherapy 26:214-228, 2006

26. Kanji S, Singh A, Tierney M, et al: Standardization of intravenous insulin therapy improves the efficiency and safety of blood glucose control in critically ill adults. Intensive Care Med 30:804-810, 2004

27. Preston S, Laver SR, Lloyd W, et al: Introducing intensive insulin therapy: The nursing perspective. Nurs Crit Care 11:75-79, 2006

28. Aragon D: Evaluation of nursing work effort and perception about blood glucose testing in tight glycemic control. Am J Crit Care 15:370-377, 2006