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REVIEW

# Blood glucose management in the patient undergoing cardiac surgery: A review

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## Abstract

Both diabetes mellitus and hyperglycemia *per se* are associated with negative outcomes after cardiac surgery. In this article, we review these associations, the possible mechanisms that lead to adverse outcomes, and the epidemiology of diabetes focusing on those patients requiring cardiac surgery. We also examine outpatient and perioperative management of diabetes with the same focus. Finally, we discuss our own efforts to improve glycemic management of patients undergoing cardiac surgery at our institution, including keys to success, results of implementation, and patient safety concerns.



**Key words:** Blood glucose management; Glycemic management; Cardiac surgery; Cardiothoracic surgery; Diabetes; Diabetes mellitus; Hyperglycemia; Perioperative

**Core tip:** There is a growing body of evidence that moderate glycemic control (*e.g.*, 120-180 mg/dL, 6.7-10.0 mmol/L) is an appropriate goal in cardiac surgery. Achieving this goal can be accomplished by adopting a multidisciplinary approach, addressing the entire continuum of care, demanding a short project timeline, and identifying gaps in current management.

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## INTRODUCTION

Diabetes is a common comorbidity in patients who require cardiovascular surgery. Worldwide, the total number of people with diabetes is projected to increase from 171 million in 2000 to 366 million in 2030[1]. According to data from the National Diabetes Fact Sheet released in January of 2011, there are 25.8 million individuals with diabetes-which is more than 8% of the population-in the United States. In addition, based on fasting blood glucose and hemoglobin A1c levels, the authors of the National Diabetes Fact Sheet estimate that there are an additional 7 million people with undiagnosed diabetes and 79 million who are prediabetic and have a greatly increased risk of developing diabetes. The American Diabetic Association and the American College of Endocrinology classify prediabetics as those individuals with fasting blood glucose levels within the 100-125 mg/dL (5.5-6.9 mmol/L) range, while those with fasting blood glucose levels greater than 126 mg/dL (7.0 mmol/L) are considered to have diabetes mellitus[2]. An estimate of the total cost of diagnosed diabetes in the United States was $245 billion in 2012: $176 billion for direct medical costs and $69 billion in reduced productivity[3]. Clearly, diabetes represents a major medical-economic problem in the developed world and the presence of diabetes complicates the management of the patient undergoing cardiovascular surgery. In this

review we will provide an overview of current data on best practices, techniques, and outcomes of glucose management in patients undergoing cardiovascular surgery. In addition, we will discuss how physicians can incorporate these findings into their own practices based on our own experiences and those of others.

## HYPERGLYCEMIA AND ADVERSE OUTCOMES

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia as a result of a deficiency in insulin secretion, an increase in insulin resistance, or a combination of both. Type 1 (or "juvenile") diabetes mellitus represents 5%-10% of all patients with the diagnosis of diabetes and is due to complete lack of insulin secretion by the pancreas. Type 2 diabetes mellitus, representing 90%-95% of all patients with the diagnosis of diabetes, is primarily due to insulin resistance resulting from multiple etiologies including genetic predisposition, unhealthy diet, lack of physical activity, and a characteristic central pattern of weight gain. Approximately 28% of diabetics will undergo coronary artery bypass grafting[4,5].

Patients with diabetes have increased morbidity and mortality following coronary artery surgery[6-8]. The incidence of stroke, renal failure, and sternal wound infections is greater in diabetic patients[9-11]. Diabetics have a 44% greater risk for readmission (following hospital discharge after coronary artery surgery) for any cause and a 24% greater risk for readmission for heart-related issues than comparable nondiabetic patients who have undergone coronary artery surgery[12,13].

## DIABETES AND CARDIAC DISEASE

Hyperglycemia and insulin resistance lead to an alteration in free fatty acid metabolism, endothelial dysfunction, and resultant thrombogenesis[14,15]. Hyperglycemia-induced endothelial dysfunction is the result of imbalance between nitric oxide bioavailability and the accumulation of reactive oxygen species, the latter triggered by activation of protein kinase C. Hyperglycemia also induces the generation of superoxide anion which inactivates nitric oxide to form peroxynitrite which induces substrate nitration[16]. Diminished nitric oxide availability is a strong predictor of adverse nitric oxide outcomes[17]. Protein kinase C also triggers the production of endothelin-1, which causes vasoconstriction, vascular inflammation and platelet aggregation[18].

Hyperglycemia results in the production of advanced glycation products (AGE) and their cell surface receptor-RAGE. RAGE contributes to the inflammatory response by activating three key transcription factors: nuclear factor κB, activated protein-1, and early growth response, all three of which are suppressed by insulin under normal conditions[19-21]. Endothelial dysfunction also results from an increase in the synthesis of vasoconstrictors and prostanoids. Increased adiposity, a common feature in diabetics, is strongly associated with increased concentrations of inflammatory markers and free fatty acids[22]. Insulin resistance also promotes atherosclerosis by increasing triglycerides, apolipoprotein B, and low-density lipoproteins. In addition, concentrations of very low-density lipoproteins are generated in response to increased synthesis of apolipoprotein B[23]. Coronary events in diabetics result from a prothrombotic state. Under normal circumstances, circulating concentrations of insulin inhibit platelet aggregation and thrombosis by inhibiting tissue factor and inhibiting production of plasminogen activator inhibitor-1 (PAI-1). In contrast, insulin resistance promotes increased synthesis of PAI-1 and fibrinogen as well as reduced production of tissue plasminogen activator. These factors collectively result in atherothrombosis[24].

Key contributors to hyperglycemia-induced vascular damage include a newly identified class of RNAs termed micro RNAs (miRNAs) which regulate gene expression at the post-transcription level[25,26]. Diabetics display a significant deregulation of the miRNAs involved in angiogenesis, vascular repair, and endothelial function[27]. Ultimately, increased oxidative vascular stress causes thrombosis, impaired platelet function, and plaque rupture-all of which will result in reduced patency of grafts, reduced ischemic events, and a greater incidence of repeat revascularization in both coronary artery disease and diabetes[28].

Hyperglycemia is associated with worse outcomes after acute coronary syndrome, acute myocardial infarction, or coronary artery surgery. Capes and coworkers performed a meta-analysis of 15 studies of patients without the diagnosis of diabetes who had glucose concentrations more than or equal to 110 mg/dL (6.1 mmol/L). Such patients had a 3.9 fold higher risk of death than patients without diabetes who had lower glucose concentrations. In patients without diabetes, glucose concentrations greater than 180 mg/dL (10 mmol/L) on admission were associated with increased risk of congestive heart failure or cardiogenic shock. Diabetic patients with glucose concentrations equal to or greater than greater than 180 mg/dL (10 mmol/L) had a moderately increased risk of death[29]. Kosiborod *et al*[30] analyzed admission glucose concentrations in 141680 elderly patients who were hospitalized for acute myocardial infarction. Twenty-six percent of these patients having glucose levels > 240 mg/dL (13.3 mmol/L) did not have the diagnosis of diabetes. Increased glucose concentrations were associated with a greater risk of 30-d mortality in patients without a previous diagnosis of diabetes (10%-39%) as compared to those patients with a diagnosis of diabetes (16%-24%)[30]. In another review of 2127 patients with acute coronary syndrome, Foo *et al*[31] showed a strong relationship between elevated glucose concentrations and an increased incidence of left ventricular failure and death. Meier *et al*[32] analyzed data from 227 type 2 diabetics and 287 nondiabetics who were diagnosed with acute myocardial infarction. Hyperglycemia at the time of myocardial infarction was associated with shorter survival, larger infarct size, and an increased incidence of adverse outcomes in both diabetics and nondiabetics[32].

Kubal *et al*[11] analyzed the association of diabetes morbidity and mortality in 6033 patients undergoing isolated coronary artery bypass surgery. Insulin dependent diabetes was associated with an increased incidence of acute renal failure (adjusted OR = 4.5), deep sternal wound infection (adjusted OR = 2.96), and prolonged postoperative stay (adjusted OR = 1.60)[11]. Gandhi *et al*[33] analyzed glucose measurements and outcomes from 409 cardiac surgery patients and found that a 20 mg/dL (1.1 mmol/L) increase in mean intraoperative glucose concentration was associated with a 30% increase of an adverse event. Doenst *et al*[34] in a retrospective review of 6280 cardiac surgery patients showed that a peak glucose of > 360 mg/dL (20.0 mmol/L) was associated with an increased likelihood of adverse events and mortality. Ascione *et al*[35] in a retrospective review of 8727 cardiac surgery patients showed that glucose level > 200 mg/dL (11.1 mmol/L) at any time during the first 5 postoperative days was associated with an increased likelihood of in-hospital morbidity and mortality. Taken together, these studies suggest that hyperglycemia during acute coronary syndromes following cardiac surgery increases the likelihood of morbidity and mortality.

The Portland Diabetic Project as described in publications by Furnary *et al*[36] provides strong evidence for an adverse linkage between hyperglycemia in diabetics undergoing cardiac surgery. This nonrandomized but prospective interventional trial involved 4864 diabetics. These investigators focused on the relationship between the use of a continuous insulin infusion and the incidence of perioperative mortality or deep sternal wound infections, and on length of hospital stay. Hyperglycemia was found to be an independent factor for increasing the likelihood of perioperative mortality. Those patients in which blood glucose remained < 150 mg/dL (8.3 mmol/L) were less likely to experience mortality (57% less likely) or deep sternal wound infections (66% less likely) as compared to diabetic patients whose blood glucose were "out of range". Butterworth *et al*[37] conducted a prospective, randomized trial of 381 nondiabetic patients undergoing cardiac surgery, where one group received a continuous insulin infusion attempting to maintain intraoperative blood glucose level less than a target level of 100 mg/dL (5.5 mmol/L) while the other group received no insulin. There was no difference in neurological or neuropsychological morbidity or in mortality between the two groups despite the insulin-receiving group having significantly lower intraoperative glucose levels[37].

Hyperglycemia associates with adverse outcomes in patients with critical illness. Van den Berghe *et al*[38] conducted a landmark study of 1548 ventilated patients. One group received insulin only if blood glucose exceeded 215 mg/dL (11.9 mmol/L) and had a target range of 180-200 mg/dL (10.0-11.1 mmol/L) while the other group received a continuous insulin infusion to maintain a blood glucose level between 80-110 mg/dL (4.4-6.1 mmol/L). Although intensive insulin therapy significantly reduced mortality in those patients requiring more than five days in the intensive care unit (ICU), there was no difference in morbidity or mortality in those with ICU stays shorter than 3 d. Bhamidipati *et al*[39] studied 4658 patients with known diabetes or perioperative hyperglycemia who were undergoing isolated coronary artery surgery. Patients in this study were stratified into a "tight group" (blood glucose concentrations < 126 mg/dL, 7.0 mmol/L), a "moderate group" (blood glucose concentrations 127-179 mg/dL, 7.0-9.9 mmol/L), and a "liberal group" (blood glucose concentrations > 180 mg/dL, 10.0 mmol/L). The moderate group had the lowest mortality 2.0% *vs* 2.9% in the tight group. Risk adjusted incidence of major complications was also less in the moderate control group suggesting that moderate control of hyperglycemia may be ideal for those diabetics undergoing isolated coronary artery surgery[39].

## OUTPATIENT DIABETES MANAGEMENT

Many patients who present for cardiac surgery have undiagnosed diabetes or metabolic syndrome. Such patients may have abnormally high blood glucose levels in the perioperative period and a significantly increased risk of adverse outcome. Of late, many institutions have formed multidisciplinary task forces involving the participation of representatives from pharmacy, anesthesiology, surgery, nursing, critical care, and endocrinology to provide better blood glucose control in patients undergoing and recovering from cardiac surgery. Some things are clear: diabetic care should be initiated in the preoperative period and not deferred until after the operation.

If possible, all cardiac surgical patients should have preoperative hemoglobin A1c (HbA1c) measurement. HbA1c levels reflect the adequacy of glycemic control in the 6-8 wk preceding the measurement. A HbA1c level of less than 7% indicates adequate glycemic control[40]. Halkos *et al*[41] found a significant association between HbA1c > 7.0% and a greater incidence of myocardial infarction, deep sternal wound infections, and mortality in patients undergoing coronary artery surgery. Some clinicians argue that elective coronary artery bypass surgery should be delayed when elevated HbA1c levels are detected to reduce the likelihood of perioperative complications. In a prospective study conducted by Lazar *et al*[42], preoperative HbA1c levels were not predictive of 30 d morbidity, length of stay, or mortality following coronary artery surgery if glycemic control was achieved. However, this was a small study ($n$ = 167) and a larger cohort would be needed to establish a definite conclusion regarding negative outcome associations with an elevated preoperative HbA1c measurement[42].

The current recommendation from the Society of Thoracic Surgeons practice guideline is that oral hypoglycemics should be withheld for at least 24 h prior to surgery. Insulin dependent diabetics should not receive their nutritional insulins (regular, aspart, glulisine, lispro) once they have begun to fast after a meal the evening prior to surgery. neutral protamine hagedorn insulin (and other

intermediate or longer-acting insulins) should be reduced (on the day of surgery) from the usual dose to avoid intraoperative hypoglycemia. Many experienced clinicians will omit all subcutaneous insulin dosing on the day of surgery and substitute intravenous insulin infusion. Patients with a blood glucose concentration greater than 180 mg/dL (10.0 mmol/L) while awaiting elective surgery should receive a continuous insulin infusion to maintain their glucose concentration below 150 mg/dL (8.3 mmol/L). Once the patient is anesthetized we recommend that blood glucose be managed as if the patients were in the critical care unit (and we do not recommend "tight" control within the limits that would be used in ambulatory practice). Intraoperative blood glucose concentrations should be measured no less frequently than hourly. Patients with abnormal kidney function should be identified preoperatively since there is a greater incidence of perioperative hypoglycemia in these patients[43,44].

## HISTORY OF PERIOPERATIVE BLOOD GLUCOSE MANAGEMENT

Perioperative management of diabetes mellitus has greatly evolved over the past several decades[45]. The scientific literature first recognized the importance of perioperative blood glucose control in the surgical patient in the early 1970s[46]. At that point, the primary concern for anesthesiologists was avoiding ketoacidosis and acute hypoglycemia. Dr. Jurgen Steinke described the common techniques employed at the time in his 1970 review. He described obtaining urine specimens every four hours perioperatively and administering "sliding scale" subcutaneous insulin based on urine glucose measurements (*e.g.*, 15 U for a 4+ urine specimen, 10 U for a 3+ urine specimen, *etc.*). Dr. Steinke recognized the many flaws of this technique, including the assumption of normal renal function and that treatment was reserved for glucosuria and not for hyperglycemia *per se*. While the deleterious effects of chronic hyperglycemia on the cardiovascular system were recognized at that time, the morbidity associated with perioperative hyperglycemia in cardiac surgery patients had not yet been appreciated. Thus, no special considerations were made for patients undergoing cardiac surgery.

Throughout the 1970s, infused insulin became more widely used in caring for the patient with critical illness[47-50]. Specifically, efforts to treat diabetic ketoacidosis with low-dose, continuous, infused insulin were met with considerable success[49]. Therefore, investigators began studying the potential role of continuous insulin in diabetic patients undergoing surgery[50]. In one report, Taitelman *et al*[50] described achieving better control of their diabetic surgical patients' blood glucose with continuous insulin infusion (as compared to conventional subcutaneous "sliding scale") as well as the unfortunate side effect of a more frequent incidence of hypoglycemia.

During the 1980s, a body of evidence was developed that linked poor glucose control in diabetics with poor wound healing and increased rates of infection[51,52]. The implications that this would have on diabetic patients undergoing surgery were clear, and by the late 1980s, algorithms for postoperative insulin infusions were widely available[53]. In 1987, Watts *et al*[53] advocated a target plasma glucose range of 120 to 180 mg/dL (6.7 to 10.0 mmol/L) at a time when ideal blood glucose ranges were not well established. As a result of the lack of consensus on so many issues related to diabetic management, there was marked variation in accepted clinical practice.

In the 1990s, a multitude of outcomes-oriented clinical trials addressing diabetes in cardiothoracic surgery patients was reported[12,54,55]. Now there was convincing evidence that diabetics were more likely to have wound infections, prolonged ICU length of stay, and mortality after cardiac surgery. Nevertheless, there remained no consensus on the ideal target range for blood glucose measurements. Consensus was reached (but only briefly) after Van den Berghe *et al*[38] 2001 prospective, randomized, controlled trial on intensive insulin therapy in 1548 critically ill patients. This study, which came to be known as the Leuven Surgical Trial, demonstrated reduced 12-mo mortality among critically ill patients when blood glucose levels were maintained in the 80-110 mg/dL (4.4-6.1 mmol/L) range as compared to 180-200 mg/dL (10.0-11.1 mmol/L). Mortality was 4.6% in the tight control group compared to 8.0% in the standard control group. The improved outcomes in the tight control group were attributed to fewer instances of multiple organ failure associated with sepsis. This led to an abrupt shift in how physicians cared for patients with critical illness. The publication of this study marked the beginning of the era of "tight control" in which standard care for critically ill patients, including those recovering from cardiothoracic surgery, mandated insulin infusion therapy.

Reports of several other important studies appeared during this time. For instance, the Portland Diabetic Project created and analyzed a large database of cardiac surgery patients ($n$ = 5510) who underwent surgery between 1987 and 2005[56]. These authors concluded that postoperative hyperglycemia rather than presence or absence of the diagnosis of diabetes was the true driver of increased mortality risk in the cardiac surgery patient. Van den Berghe *et al*[57,58] also continued to study the role of intensive insulin therapy in the critically ill during this time. In 2006, the group published two studies confirming the benefits of intensive insulin therapy in reducing the risk of morbidity and mortality in both medical and surgical ICU patients. These findings reinforced the prevailing notion that the tight control [*i.e.*, the 80-110 mg/dL (4.4-6.1 mmol/L) range that is used for tight control in ambulatory, nonsurgical practice] was also the ideal range for surgical patients in the perioperative period.

The era of tight glucose control in patients with critical illness came to an abrupt end with the publication of the NICE-SUGAR Study[59]. These investigators were famously unable to reproduce the findings of the Leuven Surgical Trial. Here, 6104 patients were randomly assigned to either intensive control (target 81 to 108 mg/dL, 4.5

to 6.0 mmol/L) or standard control [target 180 mg/dL (10.0 mmol/L) or less]. Rather than experiencing the mortality benefit that Van den Berghe *et al*[38,57,58] found, the intensive control group actually experienced a greater incidence of all-cause mortality at 90 d after surgery (27.5% mortality in intensive group *vs* 24.9% in conventional group; 95%CI for the OR = 1.02-1.28; $P = 0.02$). These results caused physicians around the world to scale back the aggressive glycemic management protocols that were instituted during the era of tight control.

More recent studies were also unable to demonstrate a benefit of tight control[60]. In 2011, Lazar *et al*[60] compared aggressive glycemic control (90-120 mg/dL, 5.0-6.7 mmol/L) against moderate control (120-180 mg/dL, 6.7-10.0 mmol/L) in 82 patients undergoing coronary artery bypass graft surgery. In this report, there was no difference in the incidence of adverse events between the groups (17 events in the moderate group compared to 15 events in the aggressive group, $P = 0.91$). Furthermore, hypoglycemic events were more frequent in the aggressive group (4 events in the moderate group compared to 30 events in the aggressive group, $P < 0.0001$). These results support the conclusions of NICE-SUGAR and suggest that moderate control (*e.g.*, 120-180 mg/dL, 6.7-10.0 mmol/L) may provide an appropriate balance between preventing adverse outcomes associated with perioperative hyperglycemia and avoiding dangerous hypoglycemic events.

## ONGOING STUDIES

Diabetes and glucose control in the patient undergoing cardiac surgery remain subjects of intense research interest. For example, ongoing studies include "improving neurologic outcomes in diabetics undergoing cardiac surgery," a clinical study ongoing at Wake Forest University (5R01HL089115). This study will address how genotype and phenotype interact to produce outcomes in patients with perioperative glucose intolerance. The hope is that with better classification of disease, management can be better tailored to meet the needs of individual patients. Ultimately, better perioperative management could lead to better perioperative glucose control and improved neurologic, neurobehavioral and other outcomes.

## CURRENT GUIDELINES

After publication of the conflicting results from the Leuven Surgical Trial and the NICE-SUGAR Study, the ideal blood glucose range for patients with critical illness (and especially patients undergoing cardiac surgery) is once again ambiguous. Nevertheless, the 2009 Society of Thoracic Surgeons (STS) Guidelines are considered the current standard[61]. The following Class I recommendations are included among these guidelines: (1) Patients taking insulin should not receive their nutritional insulin (lispro, aspart, glulisine, or regular) after receiving their dinnertime dose the evening prior to surgery (level of evidence = B); (2) Scheduled insulin therapy, using a combination of long-acting and short-acting subcutaneous insulin or an insulin infusion, should be initiated to achieve glycemic control for in-hospital patients awaiting surgery (level of evidence = C); (3) All oral hypoglycemic agents and noninsulin diabetes medications should be withheld for 24 h prior to surgery (level of evidence = C); (4) All patients with diabetes undergoing cardiac surgical procedures should receive an insulin infusion in the operating room and for at least 24 h postoperatively to maintain serum glucose levels $\leqslant$ 180 mg/dL (10.0 mmol/L) (level of evidence = B); (5) Glucose levels > 180 mg/dL (10.0 mmol/L) that occur in patients without diabetes only during cardiopulmonary bypass may be treated initially with a single or intermittent dose of intravenous (*iv*) insulin as long as levels remain $\leqslant$ 180 mg/dL (10.0 mmol/L) thereafter. However, those patients with persistently elevated serum glucose (> 180 mg/dL, 10.0 mmol/L) after cardiopulmonary bypass should receive a continuous insulin drip, and an endocrinology consult should be obtained (level of evidence = B); (6) Patients (with or without diabetes) having persistently elevated serum glucose (> 180 mg/dL, 10.0 mmol/L) should receive *iv* insulin infusion to maintain serum glucose < 180 mg/dL (10.0 mmol/L) for the duration of their ICU care (level of evidence = A); and (7) Before intravenous insulin infusions are discontinued, patients should be transitioned to a subcutaneous insulin schedule using institutional protocols (level of evidence = B).

It is important to note that these guidelines were released before the publication of the NICE-SUGAR Study, so the information available at the time would not be considered complete today. The Guidelines Writing Group at the STS is currently working on updating these guidelines.

## INSTITUTING A PERIOPERATIVE BLOOD GLUCOSE MANAGEMENT PROTOCOL

Instituting a new blood glucose management protocol can (and nearly always will) be a daunting task. While guidelines exist to define "guardrails" for insulin dosing and target glucose ranges, these guidelines provide little direction as to how best to implement the changes in practice and in culture that are so necessary to achieve those goals. Change management and the psychology of groups (particularly groups composed of "unequal" players) are beyond the scope of this manuscript[62]. These topics are covered well in any number of management textbooks and monographs. Yet, experienced clinicians will recognize the key importance of group dynamics and negotiation skills to achieving success with a new clinical strategy. In other words, these issues cannot be ignored if the new strategy will succeed. Success cannot be achieved without "buy in" from physicians on the relevant clinical services. Nevertheless, nurses will drive the protocol in the ICU and on the hospital units; nurses must be involved in program development from the start. We have seen new clinical pathways fail due to the opposition of

a single, influential, antagonistic physician. Conversely, pathway success always requires an influential, trusted, and respected champion.

McDonnell *et al*[40] published a primer in 2012 that provides some insight into the challenges that must be overcome when seeking to improve blood glucose management for cardiac surgery patients. At our institution, we encountered many of these temporary obstacles when we recently overhauled our perioperative glycemic management strategy in order to better comply with both STS Guidelines and Surgical Care Improvement Project (SCIP) requirements. We learned (or were reminded of) numerous lessons, a few of which are listed below:

### *Use a multidisciplinary approach*

As previously noted, optimal glycemic control cannot be achieved through the efforts of a single physician or single medical discipline. We formed a process improvement team with representation from cardiac surgery, cardiac anesthesia, cardiac critical care, ICU nursing, endocrinology, clinical pharmacy, dietary, and the performance improvement department. Each discipline was responsible for a small subset of the project, and frequent meetings of the entire process improvement team allowed for ongoing progress updates and collaboration.

### *Address preoperative, intraoperative, and postoperative care at the same time*

Glucose control in the preoperative, intraoperative and postoperative periods cannot be disentangled. Although it is tempting to address each stage of care in a piecemeal fashion, overall success requires the team to integrate these phases together. Having representation and periodic updates from those responsible for care at each point along the care continuum permits timely identification and remediation of persisting misconceptions or deviations from the plan.

### *Demand a relatively short project timeline (with well defined deadlines)*

Process improvement projects can (and sometimes should) go on indefinitely. But, one will never see results if a strict timeline is not enforced. We recognize that the ideal approach to process improvement (since the time of Walter Shewhart and W. Edwards Deming) is a "plan-do-study-act" repetitive cycle, but also have seen that a team can get stuck on "plan" if the focus is on perfection rather than on improvement. The perfect course of action likely will never be determined; reaching a consensus can take an exorbitantly long time when discussion and debate are allowed to continue unchecked. We structured our discussions, allowing each discipline to take the lead on the facet of the project for which they were responsible. Our process improvement team met from May 2013 to August 2013.

### *Use flow charts to facilitate identification of "gaps"*

Flow charts and process mapping were developed in industrial engineering to define precisely what is the desired "product," what are the individual steps in the process by which it is "made," who is responsible for each step, and how can we measure our success at "manufacturing" this "product?" The process improvement team "mapped" glycemic management from patient admission to discharge during its first meetings. Each discipline described in detail the manner in which care was provided within their domain. Once the entire care continuum had been described, "gaps" in ideal care were identified. For example, representatives from anesthesiology identified that they had no standard blood glucose management protocol for the intraoperative period. Representatives of the dietary department pointed out that patients who had an order for a diabetic diet could still request sugar-sweetened soft drinks during the postoperative period. Once dozens of these potential gaps had been identified, the team determined which gaps fell under the purview of which disciplines, and then voted on which gaps should be prioritized for correction. This process allowed for the systematic identification and elimination in barriers to optimal glycemic control.

## OUR SUCCESS IMPLEMENTING CHANGE

We monitored several outcome measures to evaluate the success of our newly instituted blood glucose management practices. Detailed explanations of these results are not the focus of this article, but broad trends are described here. Briefly, intraoperative blood glucose values fell within our target range 63% of the time for 35 consecutive patients who underwent cardiac surgery prior to the adoption of our new protocol. Thirty-eight consecutive patients undergoing cardiac surgery after to the institution of the protocol were similarly evaluated, and their blood glucose values fell within our target range 81% of the time ($P < 0.05$ using nonparametric tests).

Compliance with SCIP 4 measures for postoperative day one and two 6 am blood glucose values was also monitored [SCIP 4 requires postoperative day (POD) 1 and POD 2 blood glucose levels to be below 200 mg/dL]. Suboptimal performance on these measures during 2012 served as the impetus for the formation of our process improvement team. For that year, we achieved 90% compliance but lost considerable potential revenue in the value based purchasing program. For the 38 consecutive patients analyzed after the overhaul of our blood glucose management practices, we achieved 99% compliance on this SCIP 4 measure.

It is important to note that Institutional Review Board (ethics committee) approval including a waiver of consent was obtained in order to perform the chart review necessary to include these results here.

## PATIENT SAFETY AND INSULIN INFUSION

The potential dangers of insulin therapy are well known to providers, and insulin infusion in the perioperative

setting is no exception. We experienced an example of the "Swiss cheese" model of error in which a series of unexpected, sequential actions were taken; omission of any one of these actions would have prevented a protocol deviation. The individual actions leading up to this patient safety "near miss" are listed here: (1) The infusion pump was programmed for a "basic" infusion rather than using preprogrammed "guardrails" for insulin infusions. The "guardrails" settings have built-in safeguards that alert the provider when excessive doses of a drug are entered. Using the basic infusion setting circumvents these safeguards; (2) An insulin infusion was intended to be programmed for 1.5 U/h but was erroneously programmed for 105 U/h; (3) Fortunately, this programming error occurred toward the end of the case, and the error was noticed immediately upon arrival in the ICU. As a consequence, we made several changes to our intraoperative protocol: We removed decimal points from the protocol such that infusion rates are rounded to the nearest unit rather than the nearest half-unit. This allows most infusion rates to be entered as a single digit, reducing the likelihood that a three-digit infusion rate will be set accidentally; (4) The safeguards built into the "guardrails" setting are now more explicitly stated within the protocol; and (5) Initiation of insulin infusion in the operating room now requires a second provider to double-check the correctness of the infusion (just as is done prior to any blood transfusion).

Even with the most stringent safeguards in place, one must keep in mind that every time an insulin infusion is started, there is an opportunity for a life-threatening error. Despite our best intentions, human error will not soon be eliminated from health care delivery[63]. It is easy to point fingers and assign blame after a medical error, but it is far more productive to learn from mistakes and make whatever improvements are possible to the care pathways in which the error occurred.

## CONCLUSION

The association between perioperative hyperglycemia and adverse outcomes after cardiac surgery is well established. It is less clear which clinical practices will optimize outcomes in these patients: efforts to tightly control blood glucose in cardiac surgery may lead to dangerous hypoglycemia. Van den Berghe *et al*[38,57,58] showed benefits of aggressive insulin therapy to maintain tight control in the perioperative period, but later studies including NICE-SUGAR demonstrated that tight control was actually associated with worse clinical outcomes[59]. As a result, tight control is no longer standard care for patients with critical illness. Even so, a consensus regarding the range of glucose concentrations for which clinicians should be aiming in these patients has remained elusive. There is a growing body of evidence that moderate control (*e.g.*, 120-180 mg/dL, 6.7-10.0 mmol/L) is an appropriate goal. The Society of Thoracic Surgeons is expected to update their 2009 practice guidelines on perioperative glycemic management in the near future, so more formal guidance will be available at that time.

Within a given institution, selecting a target glucose range is only the first step. Implementing a protocol to achieve that goal can be a challenging ordeal, and success is more often achieved when one addresses the entire continuum of care associated with blood sugar management. It is important to obtain buy-in from all those who will be involved in the care of patients undergoing cardiac surgery. Patient safety must be paramount throughout the design of a glycemic management protocol. Human error can never be completely eliminated. Wise clinicians will respond to patient safety events as opportunities for process improvement.

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