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Review Article

# Perioperative Glycemia Control: Have We Reached the Target?

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## ABSTRACT

**Aim of review:** Perioperative hyperglycemia is very common and has been shown to be associated with increased mortality and morbidity in surgical patients, however, optimal control and management of perioperative glycemia remain uncertain.

**Methods:** We conducted a comprehensive review of current clinical strategies in perioperative glycemic control, focused on preoperative, intraoperative and postoperative glycemic control and their outcome results in the past 2 decades.

**Recent findings:** The major findings are: 1) Hyperglycemia occurs commonly during the perioperative period and is associated with increased risk for morbidity and mortality. 2) Recent clinical studies have shown that intensive or "tight" glycemic control perioperatively increase the incidence of hypoglycemia and increase mortality. 3) New clinical guidelines favor a moderate or less stringent glucose management in patients undergoing surgery.

**Conclusion:** Further studies targeting at optimal glycemic managements and improved perioperative and long-term outcomes in surgical patients remain needed. (Funded by the National Natural Science Foundation of China and Science and Technology Development Fund of Shaanxi Province, China.)


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Diabetes is a global problem with enormous medical, social and economic impact. The worldwide prevalence of diabetes has risen from 108 million (4.7% of the world population) in 1980 to 422 million (8.5% of the world population) in 2014. In the United States, in 2012, 29.1 million people or 9.3% of the population, have been diagnosed with diabetes mellitus (DM) (1); in 2013, diabetes had the highest health care spending among 155 medical conditions, with an estimated $101.4 billion in spending (2). It is estimated that more than half of diabetic patients undergo at least one surgical treatment in the lifetime (3). A recent study showed that 35.8% of patients in ICU had DM, and among them 26% had undiagnosed DM (4). Perioperative hyperglycemia is common, and it occurs in almost 30% to 40% of all surgical patients (5-7). Two-thirds of patients with DM developed perioperative hyperglycemia. In addition, patients without DM developed perioperative hyperglycemia from 13% to 67% (8). Hyperglycemia affected up to 80% of

patients undergoing cardiac surgery (9, 10), 40% of patients with acute coronary syndrome and heart failure (11), and up to 70%-90% of patients with kidney transplant postoperatively (12, 13).

## Perioperative Hyperglycemia and Its Risk

Hyperglycemia has been found to be associated with increased morbidity and mortality in hospitalized patients (14), and is recognized as a high risk factor for postoperative complications (8,15-17). These complications include increased rates of infection and major adverse cardiac events (MACEs), prolonged length of ICU stay, and increased mortality. Umpierrez et al. provided a statewide analysis including 47 hospitals, demonstrating the association of perioperative hyperglycemia and worse surgical outcomes (7). Colorectal surgery patients with postoperative blood glucose (BG) greater than 140 mg/dl was associated with 3 times increased rate of surgical site infection (SSI), compared to those having postoperative BG less than 140 mg/dl (18). In addition, patients with DM, mean BG over 200 mg/dL during the initial postoperative 48-h period had a 3.6-fold increase in the risk of SSI compared to those with mean BG under 200 mg/dL in a multivariate analysis (19). In a study, for patients with DM undergoing CABG, a change in the upper limit of glucose control from 145 mg/dL to 180 mg/dL resulted in a significantly higher rate of SSI. Subgroup analysis presented that unlike non-diabetic patients, a less stringent target was independently associated with a significant increase in the incidence of SSI from 2.2% to 6.9% for the diabetic patients (20). A study of diabetic patients who underwent total knee arthroplasty (TKA) found that, after multivariate analysis, a preoperative hemoglobin A1c (HbA1c) $\geqslant$ 8 % and/or fasting blood glucose (FBG) $\geqslant$ 200 mg/dl were associated with higher incidence of SSI (21). Perioperative hyperglycemia in cardiac surgical patients has been associated with an increased rate of deep sternal wound infections, systemic blood infections, stroke, mortality, and acute kidney injury (AKI) (22-25). In addition, perioperative hyperglycemia has also been found to significantly increase the risk of AKI in the postoperative period of non-cardiac surgical patients (5). In patients who underwent isolated CABG, perioperative mean glucose over 180 mg/dl was a significant risk factor for postoperative atrial fibrillation (AF) (26). A study of postoperative glycemic control in cardiac patients found that good glucose control, as determined by time in range (TIR), was correlated with significantly shorter cardiopulmonary bypass time (CPB), length of stay in the ICU and mechanical ventilation, and lower incidence of wound infection (27). A study focused on type 1 DM (T1DM) patients through a median follow-up of 4.7 years, confirmed that poor glycemic control (preoperative HbA1c > 8.1% ) before CABG was associated with increased long-term risk of death or MACE (28).

However, there are studies showing different results. In a large cohort of 20,171patients with total hip and knee arthroplasty procedures, after adjusting for body mass index, type of surgery, ASA score and operative time, there was no association between HbA1c values (a marker of poor or good glycemic control) and prosthetic joint infections (29). In a cohort study (n=763), neither preoperative HbA1c nor postoperative glycemic variability was found to be associated with MACEs after isolated cardiac valvular surgery (30).

Hyperglycemia has also been associated with increased risk of complications and poor outcomes in transplant patients. Kidney transplant recipients with pre-transplant DM (BG> 145 mg/dl) and new-onset DM after transplantation have been shown to have a significantly reduced graft and patients survival (31-33). During kidney transplant, early perioperative hyperglycemia has been associated with increased acute rejection episodes in patients without pre-transplant DM (13) and with increased post-operative infections (BG> 200 mg/dl) (34). A study with follow-up up to 40 months at Mayo Clinic showed that impaired fasting glucose ($\geqslant$ 110 mg/dl and < 126 mg/dl) or new-onset DM after transplantation (FBG > 126 md/dl) was associated with increased risk of coronary artery disease (CAD), peripheral vascular disease (PVD), and cerebrovascular accidents (CVA) (35). Liver transplant recipients with post-operative hyperglycemia have worse patient and graft survival because of infections, rejection, and late-onset hepatic artery thrombosis (36-38). A study of liver transplant showed that intraoperative “poor

glycemic control" (BG≥150 mg/dl and mean BG 184 mg/dl) resulted in increased rates of 30-day post-transplant infections and post-operative 1-year mortality (39). In the field of heart transplant, some studies reported similar rate of acute rejections, graft vasculopathy, infections and survival in recipients with DM (40-42), while others reported higher rates of infections, transplant CAD and decreased survival in patients

## Optimal Glucose Control

The optimal glucose management strategy during the perioperative setting remains undetermined. Optimal glucose control parameters are challenging to define due to multiple confounding factors throughout the perioperative period. There are three perioperative periods for BG control, as following (Table 1).

### Preoperative BG control

In a nationwide, cohort study including 764 patients with T1DM after CABG, with a median follow-up of 4.7 years, the hazard ratio (HR) (95% confidence intervals (CI)) for death or MACE in patients with preoperative HbA1c levels of 7.1% to 8.0%, 8.1% to 9.0%, 9.1% to 10.0%, and >10.0% were 1.34 (0.82 to 2.21), 1.59 (1.00 to 2.54), 1.73 (1.03 to 2.90), and 2.25 (1.29 to 3.94), respectively, compared with the reference category (HbA1c levels ≤ 7.0%). They concluded that in patients with T1DM, poor glycemic control (preoperative HbA1c ≥ 8.1%) before CABG was associated with increased long-term risk of death or MACE (28). Another study aimed to determine the association between preoperative medium-term (60-90 days) glycemic control, as reflected by glycosylated hemoglobin levels (HbA1c), and the incidence of major complications (mediastinitis, perioperative infarction, heart failure, stroke and kidney failure dialysis) and mortality in type II diabetic patients after CABG. This study showed that aggressive glycemic control three months before surgery, achieving HbA1c ≤ 7%, resulted in decreased morbidity and mortality (47). A 47 patients study found that, the uncontrolled diabetic group (9.1 ≤ HbA1c ≤ 10.1) before surgery had increased total protein oxidation, fibrosis, sympathetic nerve damage and decreased levels of antioxidative enzyme manganese superoxide dismutase (MnSOD), neurogenic and angiogenic markers nerve growth factor (NGF), neurotrophin (NT)-3, platelet-derived growth factor (PDGF)-β after CPB compared with the controlled diabetic group (6.0 ≤ HbA1c ≤ 6.2) or patients without DM (5.6 ≤ HbA1c ≤6.0). The investigators concluded that CPB led to higher oxidative stress in the patients with uncontrolled DM before surgical intervention, even after normal glucose levels were maintained intraoperatively. Thus, controlled HbA1c before surgery plus acute intraoperative glucose control may be a more suitable treatment for patients with DM undergoing cardiac surgery (48). A study of 528 patients with spinal cord injury (SCI) indicated that hyperglycemia on admission (BG ≥126 mg/dl) was a significant risk predictor of poor functional outcome. The authors suggested that hyperglycemia during acute SCI may be a useful prognostic factor with a negative impact on motor function, highlighted the importance of achieving tight glycemic control after central nervous system injury (49). In a study of 603 patients undergoing elective cardiac surgery, a preoperative BG >140 mg/dl was predictive of AKI following surgery (50). Additionally, several studies found that an preoperative HbA1c > 6 % has been consistently associated with higher incidence of postoperative AKI (51-53).

### Intraoperative BG control

A randomized clinical trial including 120 non-diabetic patients underwent elective CABG surgery, found that insulin infusion to maintain BG level between 110 mg/dl and 126 mg/dl in the intraoperative period leads to no hypoglycemic events and a decrease of early postoperative complications (54). A retrospective review of adult liver recipients found that intraoperative strict glycemic control (mean BG <150 mg/dl) with intravenous insulin bolus or continuous infusion, was associated with decreased rates of infection at 30 days post-transplant and 1-year mortality compared to those with poor control (mean BG >150 mg/dl), though the incidence of most postoperative complications were similar (39). A retrospective review including 880

**Table 1. Major Published Randomized Controlled Trials of Glycemic Control.**

| Study | Design | Patient Population | End Point | Results |
|---|---|---|---|---|
| van den Berghe et al. (10) | RCT | 1548 patients in surgical intensive care unit (ICU) | Mortality, complications | Intensive insulin therapy reduced morbidity and mortality among critically ill patients in the surgical intensive care unit. |
| Gandhi et al. (57) | RCT | adult patients undergoing on-pump cardiac surgery | Composite of death, sternal infections, prolonged ventilation, cardiac arrhythmias, stroke, and renal failure within 30 days after surgery | Intensive insulin therapy did not reduce perioperative death or morbidity, but with a increased incidence of death and stroke in the intensive treatment group. |
| NICE-SUGAR (60) | Large RCT | 6104 patients who admission to ICU | Death from any cause within 90 days after randomization | Intensive glucose control increased mortality among adults in the ICU. |
| NICE-SUGAR (61) | Large RCT | 6026 critically ill patients in the ICU | Death from any cause within 90 days after randomization | Intensive glucose control led to moderate and severe hypoglycemia, both of which were associated with an increased risk of death. |
| Vlasselaers et al. (66) | RCT | 317 infants (<1 yr) and 383 children (⩾1 yr) in the pediatric ICU(PICU) | Duration of PICU stay and inflammation | Targeting of blood glucose concentrations to age-adjusted normal fasting concentrations improved short- term outcome of patients in PICU. |
| Mesotten et al. (67) | RCT | 700 patients aged 16 years or younger in PICU | Intelligence, further neurodevelopmental testing encompassed tests | Children who had been treated with tight glucose control did not have a worse measure of intelligence than those who had received usual care. |
| Macrae et al. (69) | Large RCT | 1369 children (⩽16 yrs) who were admitted to the PICU | The number of days alive and free from mechanical ventilation at 30 days after randomization | Tight glycemic control in critically ill children had no significant effect on major clinical outcomes, although the incidence of hypoglycemia was higher with tight glucose control |
| SPECS (70) | RCT | 980 children (0- 36 months), undergoing surgery with cardiopulmonary bypass | The rate of health care – associated infection in the cardiac ICU, mortality, length of stay, organ failure, and hypoglycemia. | Tight glycemic control achieved a low hypoglycemia rate, but did not significantly change the infection rate, mortality, length of stay, or measures of organ failure |
| VADT (74) | Large RCT | 1791 military veterans who had a suboptimal response to therapy for type 2 diabetes | The time from randomization to the first occurrence of a major cardiovascular event, a composite of myocardial infarction, stroke, death, and amputation for ischemic gangrene | Intensive glucose control had no significant effect on the rates of major cardiovascular events, death, or microvascular event. |
| ADVANCE (75) | Mega RCT | 11,140 patients with type 2 diabetes | Composites of major macrovascular events and major microvascular events,assessed both jointly and separately | Yielded a 10% relative reduction in the combined outcome of major macrovascular and microvascular events, primarily as a consequence of a 21% relative reduction in nephropathy. |
| ACCORD (76) | Mega RCT | 10,251 patients (mean age, 62.2 years) with a median glycated hemoglobin level of 8.1% | A composite of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes | Increased mortality and did not significantly reduce major cardiovascular events. |

patients reported that the incidence of AKI was higher in patients with a intraoperative BG >

150 mg/dl than those with a intraoperative BG = 110−150 mg/dl, and coefficient of variation of glucose was an independent risk factors for postoperative AKI after off- pump CABG (55). It seems that BG <150 mg/dl is a good intraoperative glucose management strategy. However, a prospective, randomized, double- blind trial performed in Thailand found that intensive treatment with target glucose levels of 80 - 150 mg/dl lead to significantly higher incidence of hypoglycemia and similar morbidity and mortality rates compared with the conventional group (BG < 249 mg/dl) in cardiopulmonary bypass surgery patients (56). In another randomized, controlled trial from Mayo Clinic, Gandhi et al. reported that intensive insulin therapy (intraoperative BG = 4.4 (80 mg/dL) - 5.6 mmol/L (100 mg/dL)) during cardiac surgery did not reduce perioperative death or morbidity, but increased incidence of death and stroke compared with conventional treatment group (not given insulin during surgery unless intraoperative BG > 11.1mmol/L (200 mg/dL)) (57).

### Postoperative BG Control

In a retrospective study including 372 patients, authors studied continuous postoperative insulin infusion for 24 h for gynecologic oncology patients with DM and hyperglycemia with a target blood glucose of <139 ml/dl and the SSI rates. They found that, after multivariate analysis, intensive glycemic control for 24 h after gynecologic oncology surgery in patients with DM and postoperative hyperglycemia lowered the SSI rate by 35% (58). As described above, in patients with CABG, postoperative atrial fibrillation (AF) often occurred in patients with high postoperative BG and a strong positive correlation existed between the time of the maximum postoperative BG and AF onset time (P = 0.746) (26). A study focused on CABG patients in the local Southeast Asian population found that, a less stringent target from 4-8 mmol/L (72 − 145 mg/dl) to 4-10 mmol/L (72 − 180 mg/dl) was independently associated with a significant increase in the incidence of SSI from 2.2% to 6.9% for the diabetic patients (20).

Many studies have been completed assessing postoperative glycemic control, thus far, the most important ones are the Leuven Surgical Trial reported in 2001 by Van den Berghe et al. and the NICE- SUGAR trial reported in 2009 by NICE- Sugar study investigators led by Simon Finfer et al. In 2001, the prospective, randomized, controlled Leuven Surgical Trial triggered the treatment protocol that favored intensive glucose control (10). There were 1,548 patients in the surgical ICU in the study, 63% of them underwent cardiac surgery, and 13% of them were DM patients. Insulin infusions were adjusted to maintain a range of 180 to 200 mg/dl for the conventional group and 80 to 110 mg/dL for the intensive group. Compared with conventional glucose control, intensive glucose control showed reduced length of ICU stay, mechanical ventilation, sepsis, and led to a reduction in mortality (10). Since then, many investigators have examined hyperglycemia treatment protocols, in particular, the intensive glycemic control (3,8,9, 14,59). A turning point occurred in 2009 when the landmark clinical trial, NICE-SUGAR study was published. This prospective, multicenter, randomized controlled trial included 6,104 patients (37% surgical patients) and found that intensive glucose control (BG = 81-108 mg/dl) actually increased 90-day mortality in medical and surgical ICU patients compared with conventional glucose control (BG < 180 mg/dl), although there was no significant difference between the two treatment groups in the ICU or hospital stay, mechanical ventilation and renal-replacement therapy (60). In a subsequent study, the NICE-SUGAR study investigators examined the associations between moderate and severe hypoglycemia (blood glucose, 41 to 70 mg/dl [2.3 to 3.9 mmol/l] and ⩽ 40 mg/dl [2.2 mmol/l], respectively) and death among 6,026 patients in ICU and they found that intensive glucose control in critically ill patients led to moderate and severe hypoglycemia, both of which were associated with an increased risk of death (61).

## Optimal Glucose Control for Special Patients

A retrospective cohort study (n = 9,838) of selected adverse pregnancy outcomes among untreated gestational diabetic women found that, after adjustment for confounders, women with fasting BG > 95 mg/dl, 1-hour BG > 191 mg/dl, or 2-hour BG > 162 mg/dl were at significantly

greater risks for preeclampsia or eclampsia, preterm delivery, primary cesarean delivery, shoulder dystocia, higher birth weight, ponderal index, large for gestational age, transient tachypnea, and neonatal hypoglycemia than women without gestational DM (62).

Hyperglycemia is also prevalent in pediatric patients with critical illness or following cardiac surgery and it is associated with worse outcomes, even in those children with previously normal glucose homeostasis (63,64). The degree of hyperglycemia has been associated with adverse outcome in pediatric cardiac surgery patients (65). A study by Vlasselaers et al., including 700 critically ill pediatric patients, studied whether glycemic control in the pediatric cardiac surgery population during the perioperative period is as beneficial as shown in the adult population. Patient were randomized to receive glycemic control to obtain age-adjusted normoglycemia (50-80 mg/dl (2.8-4.4 mmol/L) in infants and 70-100 mg/dl (3.9-5.6 mmol/L) in children) or to tolerating hyperglycemia up to 215 mg/dL (11.9 mmol/L). Glycemic control in this pediatric ICU population reduced the inflammatory response, the postoperative levels of troponin and heart-type fatty acid binding protein (H-FABP, used for the early diagnosis of myocardial infarction), the rate of secondary infections, ICU stay, and improved ICU survival. The occurrence of hypoglycemia increased in the glycemic control group, but did not have a negative effect on the acute outcomes (66). Additionally, glycemic control had a positive effect on cognitive executive functions after 4 years follow up, such as motor coordination and cognitive flexibility (67). The same investigators group showed that targeting age-adjusted normoglycemia during and after cardiac surgery in neonates (50-80 mg/dl) protected the myocardium and reduced the inflammatory response (68). However, two large randomized control trials, the CHiP and the SPECS trials, showed no clinical benefits from tight glycemic control in pediatric patients following cardiac surgery against their primary endpoints (69, 70), although different results have been reported in other trials in pediatric patients (66,71). There are wary among ICU physicians about the risk of severe hypoglycemia associated with tight glycemic control in pediatric patients. Previous studies showed that hypoglycemia was not associated with a risk of neurocognitive disability in a 4-year follow-up study (67), but was associated with an increased mortality (72).

The prevalence of T2DM increases with age. In addition, elderly patients with DM have higher rates of comorbidities, involving the heart, kidneys, brain, peripheral arteries and others (73). Lately 3 large clinical trials, Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE), Veterans Affairs Diabetes Trial (VADT), and Action to Control Cardiovascular Risk in Diabetes (ACCORD), evaluated the intensive glucose control vs the standard glucose control (HbA1c goals were: 6.0% vs 7.0% – 7.9%) (74-76). None of the 3 trials showed any benefit of intensive glucose lowering on the reduction of cardiovascular risk with following-up to 5 years, with the ACCORD trial being terminated early due to excess mortality among the intensively treated group (74-76). A tighter glycemic control with HbA1c < 7.0% may not be appropriate for older patients due to the risk of severe hypoglycemia. Currently an HbA1c target between 7.5%-9% will increase benefits and reduce harms for the majority of older patients. Perioperatively, high-quality evidence about glycemic control in older patients is lacking. The more conservative control, in particular, to monitor and prevent server hypoglycemia should be made in older patients undergoing surgery.

The concept of enhanced recovery after surgery (ERAS) was first advanced among colorectal surgeries in the early 2000s. ERAS promotes implementing a bundle of care interventions targeted to improve recovery following surgery. Recognizing the association of hyperglycemia with poor outcomes, many ERAS programs include glycemic control interventions. A recent meta-analysis showed that in patients undergoing colorectal surgery, surgical care bundle with core interventions including antibiotic administration, appropriate hair removal, glycemic control and normothermia, significantly reduced the risk of SSI (77).

## Conclusions

In summary, more than a decade has passed

**Table 2. Current Recommendations for Glycemic Control.**

| Society, Guidelines | Patient Group | Target Range | Rational |
|---|---|---|---|
| American Association of Clinical Endocrinologists (AACE) and American Diabetes Association (ADA), Consensus Statement on Inpatient Glycemic Control (2009) (14) | Critical ill patients | 140 - 180 mg/dl | Insulin therapy should be initiated for treatment of persistent hyperglycemia, starting at a threshold of no greater than 180 mg/dl (10.0 mmol/L).<br>Once insulin therapy has been started, a glucose range of 140 – 180 mg/dl (7.8 – 10.0 mmol/L) is recommended for the majority of critically ill patients.<br>Intravenous insulin infusions are the preferred method for achieving and maintaining glycemic control in critically ill patients.<br>Validated insulin infusion protocols with demonstrated safety and efficacy, and with low rates of occurrence of hypoglycemia, are recommended.<br>With IV insulin therapy, frequent glucose monitoring is essential to minimize the occurrence of hypoglycemia and to achieve optimal glucose control. |
| American Association of Clinical Endocrinologists (AACE) and American Diabetes Association (ADA), Consensus Statement on Inpatient Glycemic Control (2009) (14) | Noncritical ill patients | 140 - 180 mg/dl | For the majority of noncritically ill patients treated with insulin, the premeal BG target should generally be 140 mg/dl (7.8 mmol/L) in conjunction with random BG values 180 mg/dl (10.0 mmol/L), provided these targets can be safely achieved.<br>More stringent targets may be appropriate in stable patients with previous tight glycemic control.<br>Less stringent targets may be appropriate in terminally ill patients or in patients with severe comorbidities.<br>Scheduled subcutaneous administration of insulin, with basal, nutritional, and correction components, is the preferred method for achieving and maintaining glucose control.<br>Prolonged therapy with sliding scale insulin (SSI) as the sole regimen is discouraged.<br>Noninsulin antihyperglycemic agents are not appropriate in most hospitalized patients who require therapy for hyperglycemia.<br>Clinical judgment and ongoing assessment of clinical status must be incorporated into day-to-day decisions regarding treatment of hyperglycemia. |
| The Society of Thoracic Surgeons Practice Guideline (2009) (78) | Cardiac surgery patients | < 180 mg/dl | Reduces mortality, morbidity, hospital length of stay;<br>Lowers the incidence of wound infections;<br>Enhances long-term survival. |
| The Amerivan College of Physicians (ACP) Guideline (2011) (79) | Adults with inpatient hyperglycemia | 140 - 200 mg/dl | ACP recommends not using intensive insulin therapy to strictly control blood glucose in non-surgical intensive care unit (SICU)/medical intensive care unit (MICU) patients with or without diabetes mellitus (Grade: strong recommendation, moderate-quality evidence).<br>ACP recommends not using intensive insulin therapy to normalize blood glucose in SICU/MICU patients with or without diabetes mellitus (Grade: strong recommendation, high-quality evidence).<br>ACP recommends a target blood glucose level of 7.8 to 11.1 mmol/L (140 to 200 mg/dL) if insulin therapy is used in SICU/MICU patients (Grade: weak recommendation, moderate-quality evidence). |

since Leuven study in 2001 (10). Previous studies and guideline recommendations had favored tight glycemic control until the landmark NICE SUGAR study in 2009 (60), which ended a "sweet dream" with the major findings: namely intensive glucose control increased the incidence of moderate to severe hypoglycemia and increased mortality among adults in the ICU. Since then, guidelines have been changed to favoring less stringent BG control (Table 2). For adult cardiac surgery patients, the Society of Thoracic Surgeons (STS) recommends continuous insulin infusion with a treatment goal of glucose <180 mg/dl during surgery (78). The American Diabetes Association (ADA) and American Association of Clinical Endocrinologists (AACE)

recommend initiating insulin therapy for glucose >180 mg/dl with a target level of 140 to 180 mg/dl. Under this guideline, they suggest that more stringent targets may be appropriate in stable patients with previous tight glycemic control (14). The American College of Physicians recommends against intensive insulin control and suggests a target glucose of 140 to 200 mg/dl (79). The Critical Care Society recommends that a blood glucose ⩾ 150 mg/dl triggers interventions to maintain blood glucose below that level and absolutely < 180 mg/dl (80). The latest clinical trials showed that in patients with T1 DM who received multiple daily insulin injections, the use of continuous glucose monitoring (CGM) compared with usual care limited hyperglycemia and hypoglycemia, improved diabetes control and reduced glucose variability (81,82). However, it remains to be examined on whether CGM improves the long- term outcomes and whether it is practical (its potential utility) for both T1 and T2 DM patients. Future clinical studies in the area of perioperative glycemia control should have a balanced approach that treat and control hyperglycemia while monitoring and preventing, in particular, moderate (BG 41-70 mg/dl) and severe hypoglycemia (BG ⩽ 40 mg/dl). In addition, the mechanism studies should address whether hyperglycemia is a surrogate maker or a true cause for adverse outcomes.

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