Society for Ambulatory Anesthesia Consensus Statement on Perioperative Blood Glucose Management in Diabetic Patients Undergoing Ambulatory Surgery

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Optimal evidence-based perioperative blood glucose control in patients undergoing ambulatory surgical procedures remains controversial. Therefore, the Society for Ambulatory Anesthesia has developed a consensus statement on perioperative glycemic management in patients undergoing ambulatory surgery. A systematic review of the literature was conducted according the protocol recommended by the Cochrane Collaboration. The consensus panel used the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system for providing suggestions. It was revealed that there is insufficient evidence to provide strong recommendations for the posed clinical questions. In the absence of high-quality evidence, recommendations were based on general principles of blood glucose control in diabetics, drug pharmacology, and data from inpatient surgical population, as well as clinical experience and judgment. In addition, areas of further research were also identified. (Anesth Analg 2010;111:1378–87)

Given the escalation in the prevalence of diabetes mellitus worldwide and a significant increase in surgical procedures performed on an outpatient basis, anesthesiologists will encounter diabetic patients in the ambulatory setting with increasing frequency. Surgical stress response can lead to relative insulin deficiency through increased insulin resistance and reduced insulin secretion, which elevate blood glucose levels.[1] Hyperglycemia in the perioperative period can cause dehydration, fluid shifts, electrolyte abnormalities, a predisposition to infection, and impaired wound healing, as well as ketoacidosis and hyperosmolar states.[1]

In critically ill patients and in patients undergoing major surgical procedures, hyperglycemia may be associated with increased perioperative morbidity and mortality.[1] However, several randomized controlled trials (RCTs) evaluating tight perioperative glycemic control (blood glucose levels between 80 and 110 mg/dL) have reported inconsistent results, including some studies reporting harm to the patients.[1–3] In addition, tight control demands frequent measurements of glucose levels, which may further increase the complexity of perioperative glucose management. Nevertheless, tight glycemic control during the perioperative period has been recommended by several professional organizations and has been targeted as a national quality improvement initiative by the Centers for Medicare and Medicaid Services.[4]

Although a recent consensus statement of the American Association of Clinical Endocrinologists (AACE) and the American Diabetes Association (ADA) issued clinical recommendations for the management of hyperglycemia in hospitalized patients, including the critically ill and those undergoing major surgical procedures; perioperative blood glucose control in patients undergoing ambulatory surgical procedures was not addressed.[5]

On the basis of the demands from members of the Society for Ambulatory Anesthesia (SAMBA), the Task Force on Clinical Practice Guidelines developed a consensus statement on perioperative glycemic management in patients undergoing ambulatory surgery. In approving this document as a consensus statement, a similar process was used as created by the SAMBA Board of Directors for the development of the SAMBA consensus guidelines for the management of postoperative nausea and vomiting.[6]

METHODS

A systematic review of the literature concerning perioperative blood glucose management in adult patients undergoing ambulatory surgery was conducted according to the protocol recommended by the Cochrane Collaboration.[7] We searched the Cochrane Controlled Trials Register, the Cochrane Library (Issue 4, 2009), MEDLINE, and EMBASE from January 1980 to November 2009. A reference librarian familiar with literature search protocol of the Cochrane Collaboration (Marina Englesakis, Toronto, Ontario, Canada) designed and conducted the electronic search strategy

Table 1. Level of Evidence

Category 1	High-level evidence (i.e., high-powered randomized clinical trials or meta-analyses), and the panel has reached uniform (near unanimous) consensus.
Category 2A	Lower-level evidence (phase II or large cohort studies), but despite the absence of higher-level studies, there is uniform consensus that the recommendation is appropriate. It is assumed that these recommendations may be modified as higher-level evidence becomes available.
Category 2B	Lower-level evidence, and there is nonuniform consensus that the recommendation should be made. This suggests to the practitioner that there could be more than one approach to the question in statement.
Category 3	A major disagreement among the panel members. The level of evidence is not pertinent in this category, because experts can disagree about the significance of high-level trials. This category directs the practitioners that there is a major interpretation issue in the data and directs them to the manuscript for an explanation of the controversy.

with input from members of the consensus panel. The following keywords were used to develop the search strategy: "diabetes mellitus," "hyperglycemia," "insulin," "hypoglycemic agents," "NIDDM," "DM," "IDDM," "blood glucose," "intraoperative," "postoperative," "perioperative," "preoperative," "surgery," "surgical procedures," "outpatient," and "ambulatory." Of note, anesthetic management of diabetic patients is not reviewed.

We hand-searched reference lists from the already retrieved articles to identify further trials. The search was limited to only English language and human trials. The librarian deleted duplicate records. The search results were screened by the authors in a stepwise manner to identify the eligible studies. In the first step we screened the titles, and irrelevant papers were excluded. In the next step, we read the abstract or full text of the papers for inclusion. The number of and reason for excluded studies in this step was recorded. We selected all reviews, trials, or RCTs of ambulatory surgical procedures in which perioperative management of adult (age ≥18 years) diabetic patients was studied.

The recommendations were formulated by the consensus group, using the Delphi method to collate rounds of individual comments on the evidence and draft recommendations, followed by roundtable discussions and then further Delphi rounds to achieve final consensus.[8] The benefits and risks of interventions and clinical practice information were considered to ensure that the recommendations maintain patient safety and have clinical validity and usefulness. The categories of evidence were based upon the level of evidence and agreement among the members of the consensus panel (Table 1).

We used the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system for grading the recommendations.[9–11] The strength of recommendations was graded either as "strong" or "weak." A strong recommendation was offered when the desirable effects of an intervention clearly outweighed or clearly did not outweigh the undesirable effects. A weak recommendation was offered if the overall effects were less certain, either because of low-quality evidence or because evidence suggested that desirable and undesirable effects were closely balanced.

The consensus panel considered the following clinical questions:

1. What, if any, preoperative information specifically related to glycemic control should be obtained about diabetic patients?
2. How do we manage preoperative oral antidiabetic and noninsulin injectable therapy?
3. How do we manage preoperative insulin therapy?
4. Is there a preoperative blood glucose level above which one should postpone elective surgery?
5. What is the optimal intraoperative period blood glucose level?
6. How do we maintain optimal blood glucose levels?
7. Should an insulin-naïve patient receive insulin to optimize blood glucose levels?
8. What are the other considerations specific to glycemic control in diabetic outpatients?
9. What is the optimal perioperative blood glucose monitoring?
10. How should we identify and manage perioperative hypoglycemia?
11. What are the discharge considerations for diabetic outpatients?
12. What advice should we give to patients for glucose control after discharge home?
13. What are the areas for future research?

RESULTS

The Quality of Reporting of Meta-analysis (QUORUM) guidelines were followed for the description of this study (Fig. 1). We screened 8488 abstracts yielded by our search strategy; after title review, 8179 irrelevant studies were excluded and 309 studies were considered for inclusion, but 299 studies were subsequently excluded for reasons that are given in detail in Figure 1. We eventually included only 1 systematic review and 9 trials including 5 RCTs.[12–21]

Overall, studies evaluating perioperative glycemic control in patients undergoing ambulatory surgery are sparse and of limited quality. Thus, there is insufficient evidence to provide strong recommendations for the posed questions regarding perioperative blood glucose management of diabetics undergoing ambulatory surgery. In the absence of high-quality evidence, recommendations were based on general principles of blood glucose control in diabetics, drug pharmacology, data from inpatient surgical population, and review articles,[22–32] as well as clinical experience and judgment.

DISCUSSION

In an ambulatory surgery setting, the primary goals are the avoidance of hypoglycemia and maintenance of adequate blood glucose control. This is accomplished with minimal disruption in the patients' antidiabetic therapy, frequent blood glucose monitoring, and prompt resumption of oral intake after the surgery.
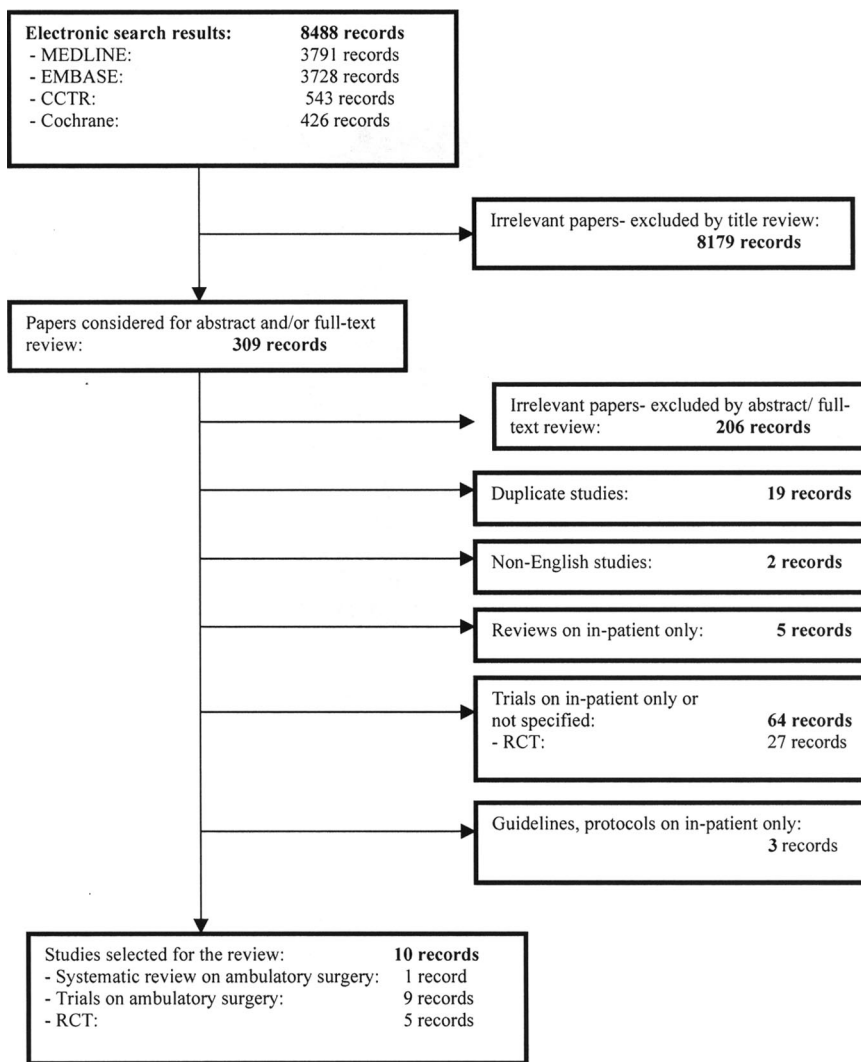
Figure 1. Flowchart of the literature search and study selection. Numbers in boldface type are to be added; other numbers may overlap. RCT = randomized controlled trials; CCTR = Cochrane Controlled Trials Register.

What, if Any, Preoperative Information Specifically Related to Glycemic Control Should Be Obtained About Diabetic Patients?

With regard to blood glucose management, preoperative evaluation may include the level of glycemic control (as is assessed by blood glucose levels and glycosylated hemoglobin A1c [HbA1c]). The HbA1c reflects the average glycemic levels over the previous 3 to 4 months and therefore is a good indicator of long-term glycemic control. The evaluation should also include the type and dose of antidiabetic therapy (i.e., oral antidiabetics and insulin), the occurrence and frequency of hypoglycemia, the manifestations of hypoglycemia and blood glucose level at which hypoglycemic symptoms occur, and hospital admissions due to glycemic control issues. The ability of the patient to reliably test blood glucose levels as well as to understand and manage diabetes should also be noted, because this would guide perioperative treatment goals.[5]

How Do We Manage Preoperative Oral Antidiabetic and Noninsulin Injectable Therapy?

There is insufficient evidence regarding preoperative management of oral antidiabetics. The pharmacology of oral antidiabetics (Table 2) and noninsulin injectables (Table 3) suggests that hypoglycemia rarely occurs with these medications, except occasionally with sulfonylureas, meglitinides, and noninsulin injectables.[22,23,32–35] In addition, there is no evidence that metformin is associated with an increased risk of perioperative lactic acidosis (level of evidence [LoE] category 1).[36,37] Nevertheless, in patients with renal dysfunction and those who might receive IV contrast, metformin may be discontinued 24 to 48 hours before surgery.

Overall, it may not be necessary to discontinue oral antidiabetics before the day of surgery (LoE category 2A). However, we suggest that oral antidiabetics and noninsulin injectables should not be taken on the day of surgery (LoE category 2A) until normal food intake is resumed.

How Do We Manage Preoperative Insulin Therapy?

There is insufficient evidence regarding preoperative management of insulin. In the absence of evidence, patient instructions regarding preoperative insulin use should be based on safety concerns (i.e., avoidance of hypoglycemia) as well as maintenance of adequate glucose control. Suggestions for perioperative insulin use are based upon principles for insulin administration to maintain blood

Table 2. Pharmacology of Oral Antidiabetic Agents

Drug class: generic (trade name)	Mechanism of action	Half-life (hours)	Adverse effects

Biguanides
  Metformin (Glucophage)
  Metformin extended release
	Decrease hepatic gluconeogenisis, increase insulin sensitivity.	6–18
		24
			Diarrhea, nausea, vomiting, lactic acidosis (avoid in renal & liver disease, congestive heart failure).

Sulphonylureas
  Chlorpropamide (Diabenese)
  Tolbutamide (Orinase)
  Glimepride (Amaryl)
  Glipizide (Glucotrol)
  Glyburide (DiaBeta, Micronase)
	Stimulate insulin secretion, decrease insulin resistance.	2–10	Hypoglycemia (caution in elderly & renal disease). Gastrointestinal disturbance.

Meglitinides
  Repaglinide (Prandin)
  Nateglinide (Starlix)
	Stimulate pancreatic insulin secretion.	1	Hypoglycemia, but less common in comparison with sulfonylureas.

Thiazolidindiones
  Rosiglitazone (Avandia)
  Pioglitazone (Actos)
	Regulate carbohydrate and lipid metabolism, reduce insulin resistance and hepatic glucose production.	3–8	Fluid retention, increased cardiac risk including congestive heart failure. Hepatotoxicity.

Alpha-glucosidase inhibitors
  Acarbose (Precose)
  Miglitol (Glyset)
	Reduce the intestinal absorption of ingested glucose.	2–4	Gastrointestinal irritation, flatus.

Dipeptidyl peptidase-4 (DPP-4) inhibitors
  Sitagliptin (Januvia)
  Saxagliptin (Onglyza)
	Reduces breakdown of gastrointestinal hormone-incretins (glucagon-like peptide type-1, enhance insulin secretion, decrease glucagon.	8–14	Infection.

Table 3. Noninsulin Injectables

Drug class: generic (trade name)	Mechanism of action	Half-life (hours)	Adverse effects
Exenatide (Byetta)	Synthetic form of exendin 4, which has actions similar to glucagon-like peptide type-1 (GLP-1). Suppresses glucagon secretion and hepatic glucose production. Suppresses appetite. Delays gastric emptying.	6–10	Nausea, vomiting, weight loss, hypoglycemia when combined with sulfonylureas.
Pramlintide (Symlin)	Synthetic form of amylin, a naturally occurring peptide that is cosecreted with insulin by beta cells. Suppresses postprandial glucagon secretion and hepatic glucose production. Enhances the effects of insulin. Suppresses appetite. Delays gastric emptying.	2–4	Nausea, vomiting, weight loss, hypoglycemia with insulin.

glucose control, which mimics physiologic insulin release consisting of both a basal component (targeting fasting or interprandial [between meals] hyperglycemia) and a correction component (targeting postprandial hyperglycemia). Basal glycemic control is usually accomplished by using long- or intermediate-acting insulin or continuous subcutaneous insulin infusion of rapid-acting insulin delivered via an insulin pump. Postprandial glycemic control is usually accomplished by using short-acting or rapid-acting insulin (Table 4). The basal-bolus insulin regimens have been used with increasing frequency in recent years.[22–24]

Because basal insulin regimens are generally used to maintain blood glucose control between meals, patients should not experience hypoglycemia with these regimens, even if meals are missed (e.g., during preoperative and postoperative fasting). Thus, there should be minimal alterations in the basal insulin doses on the day before surgery unless the patient reports a history of hypoglycemia at night, in the morning, or with missed meals and in patients on diet restriction preoperatively (e.g., bowel preparation). On the other hand, patients using insulin in combination with oral antidiabetics[38] or regimens using intermediate-acting insulins with a peak effect (e.g., NPH, Lente, and Protamine lispro) may experience hypoglycemia, if a meal is omitted.[25,39]

Plans for preoperative insulin management should consider the level of preoperative glycemic control (i.e., fasting blood glucose level and HbA1c); for example, patients with tight glycemic control or those with a wide range of daily blood glucose values and those using complex insulin regimens are more likely to experience hypoglycemia if meals are omitted. Patients' ability to check blood glucose levels and follow instructions regarding appropriate dose adjustments is critical in avoiding hypoglycemia. In addition, the timing of surgery and the expected time to

Table 4. Pharmacology of Insulin

Drug class: generic (trade name)	Onset	Peak effect	Duration
Short acting and rapid acting			
Regular (Novolin R, Humulin R)	30–60 minutes	2–4 hours	6–8 hours
Lispro (Humalog)	5–15 minutes	30–90 minutes	4–6 hours
Aspart (Novolog)	5–15 minutes	30–90 minutes	4–6 hours
Glulisine (Apidra)	5–15 minutes	30–90 minutes	4–6 hours
Intermediate acting			
NPH (Novolin N, Humulin N-NF)	2–4 hours	4–10 hours	10–16 hours
Zinc insulin (Lente)	2–4 hours	4–10 hours	12–20 hours
Extended zinc insulin (Ultralente)	6–10 hours	10–16 hours	18–24 hours
Long acting (peakless)			
Glargine (Lantus)	2–4 hours	None	20–24 hours
Detemir (Levemir)	2–4 hours	None	20–24 hours
Mixed insulins (NPH + regular)			
70% NPH/30% regular (Novolin 70/30, Humulin 70/30)	30–90 minutes	Dual	10–16 hours
50% NPH/50% regular (Humulin 50/50)	30–90 minutes	Dual	10–16 hours
Mixed insulins (intermediate-acting + rapid-acting analogs)			
70% Aspart Protamine suspension/30% Aspart (Novolog mix 70/30)	5–15 minutes	Dual	10–16 hours
75% Lispro Protamine suspension/25% Lispro (Humalog mix 75/25)	5–15 minutes	Dual	10–16 hours
50% Lispro Protamine suspension/50% Lispro (Humalog mix 50/50)	5–15 minutes	Dual	10–12 hours

Table 5. Instructions to Patient Regarding Preoperative Insulin and Noninsulin Injectable Administration

Insulin regimen	Day before surgery	Day of surgery	Comments
Insulin pump	No change	No change	Use "sick day" or "sleep" basal rates.
Long-acting, peakless insulins	No change	75%–100% of morning dose	Reduce nighttime dose if history of nocturnal or morning hypoglycemia. On the day of surgery, the morning dose of basal insulin may be administered on arrival to the ambulatory surgery facility.
Intermediate-acting insulins	No change in the daytime dose. 75% of dose if taken in the evening	50%–75% of morning dose	See the comments for long-acting insulins.
Fixed combination insulins	No change	50%–75% of morning dose of intermediate-acting component	Lispro-protamine only available in combination; therefore use NPH instead, on day of surgery. See the comments for long-acting insulins.
Short- and rapid-acting insulin	No change	Hold the dose	
Noninsulin injectables	No change	Hold the dose	

resumption of regular diet after surgery should also be considered. The suggestions for preoperative insulin administration are included in Table 5 (LoE category 2A).

Is There a Preoperative Blood Glucose Level Above Which One Should Postpone Elective Surgery?

There are insufficient data to specifically recommend the level of preoperative fasting blood glucose or HbA1c levels above which elective ambulatory surgery should be postponed. In addition to inadequate long-term glycemic control, preoperative hyperglycemia is commonly due to inappropriate discontinuation of preoperative antidiabetic therapy and preoperative stress response. Surgery should be postponed in patients with significant complications of hyperglycemia such as severe dehydration, ketoacidosis, and hyperosmolar nonketotic states (LoE category 2A).[1]

It may be acceptable to proceed with surgery in patients with preoperative hyperglycemia but with adequate long-term glycemic control (LoE category 2A). The ADA recommends that outpatient management of diabetes should ideally include a combination of a target HbA1c <7% (normal 4%–7%), a preprandial blood glucose level of 90 to 130 mg/dL and a peak postprandial blood glucose level of <180 mg/dL,[22] although this has not been verified in the ambulatory surgical population.

In chronically poorly controlled diabetic patients, the decision to proceed with ambulatory surgery should be made in conjunction with the surgeon while taking into consideration the presence of other comorbidities and the potential risks of surgical complications (e.g., delayed wound healing and wound infection). There are no RCTs evaluating the effects of preoperative glycemic control on postoperative infection in ambulatory surgical procedures.[40] However, a review of outcomes after noncardiac surgery found that HbA1c <7% was associated with a significantly lower incidence of postoperative infections.[41]

What Is the Optimal Intraoperative Blood Glucose Level?

There is no evidence in the literature that any particular blood glucose level is either beneficial or harmful for patients undergoing ambulatory surgical procedures. Therefore, the optimal blood glucose level for ambulatory surgical patients remains unknown. In the absence of direct

evidence, suggestions are based on data from hospitalized surgical patients and a consensus statement of the AACE/ADD.[5] We suggest that in patients with well-controlled diabetes, intraoperative blood glucose levels be maintained <180 mg/dL (10.0 mmol/L) (LoE category 2A). Of note, the selection of perioperative blood glucose level should depend upon the duration of surgery, invasiveness of surgical procedure, type of anesthetic technique, and expected time to resume oral intake and routine antidiabetic therapy. For example, higher blood glucose levels may be acceptable in patients undergoing short surgical procedures after which patients are promptly expected to resume oral intake and antidiabetic therapy.

However, in patients with poorly controlled diabetes, if the decision to proceed with the surgery is made, the blood glucose levels should be maintained around their preoperative baseline values rather than temporarily (i.e., perioperatively) normalizing them (LoE category 2A). Chronically elevated blood glucose levels should not be decreased acutely in the perioperative period because the threshold at which a patient experiences symptoms or organ impairment due to hypoglycemia is dynamic and varies with their long-term glycemic control.[22,25] Patients with poorly controlled type 2 diabetes have an altered counterregulatory response (i.e., release of epinephrine, norepinephrine, growth hormone, cortisol, and pancreatic polypeptide), resulting in hypoglycemic symptoms at normal blood glucose levels.[42–44] Also, significant fluctuations in blood glucose levels caused by acute reduction in chronically elevated blood glucose levels can lead to detrimental biochemical effects including increased oxidative stress response[45] and may increase perioperative morbidity and mortality.[1,46]

How Do We Maintain Optimal Blood Glucose Level?

There are insufficient data regarding the best strategy or regimen to attain target blood glucose levels in ambulatory surgical patients with diabetes mellitus. The type, dose, and route of administration of insulin used to maintain an optimal blood glucose level are discussed below.

Type of insulin (regular insulin vs. rapid-acting insulin). There is not enough evidence at this time to recommend the use of one type of insulin in preference of another, because there are no studies comparing regular insulin with rapid-acting insulins in ambulatory surgical patients. However, for subcutaneous dosing, rapid-acting insulins have superior pharmacokinetics in comparison with regular insulin (Table 4). Studies in patients with diabetic ketoacidosis demonstrated that subcutaneous doses of rapid-acting insulin administered every 1 to 2 hours closely matched IV infusion of regular insulin with respect to efficacy and safety.[47,48] In addition, the use of a subcutaneous rapid-acting insulin approach was less labor-intensive and thus more cost effective. Another benefit of using rapid-acting insulin is that it may reduce the duration of observation required in the postoperative period because the peak blood levels are achieved earlier than with regular insulin (see the Discharge section). Therefore, in an ambulatory setting, subcutaneous rapid-acting insulin analogs may be preferred over regular insulin (LoE category 2A).

Route of insulin administration (IV vs. subcutaneous). Because IV bolus doses of insulin have a very short duration of action (30 to 40 minutes), which can cause significant fluctuations in blood glucose levels that could be detrimental to the patients,[31] it is not recommended (LoE category 2A).

Although IV infusion of regular insulin has been used to maintain optimal blood glucose levels in patients undergoing major surgical procedures and in critically ill patients, the AACE/ADA consensus statement recommends the subcutaneous route for noncritical patients.[5] IV insulin infusion requires more frequent monitoring because there are concerns of hypoglycemia. Overall, insulin infusion may not be necessary or practical in the outpatient surgical setting. Furthermore, as is mentioned above, subcutaneous administration of rapid-acting insulin has been shown to provide similar control as IV infusion of regular insulin.[47,48] Therefore, subcutaneous administration is the preferred method for achieving and maintaining target glucose levels (LoE category 2A).

Of note, one of the concerns with subcutaneous administration is the possibility of "stacking" of repeated doses, which may result in hypoglycemia. Thus, additional subcutaneous doses of insulin should not be administered until the time to peak effect has passed or blood glucose is being closely monitored.

Dosing schedule. There is not enough evidence to recommend a dosing schedule to optimize the blood glucose levels. There are no validated insulin administration protocols that have been shown to be safe and effective in ambulatory surgical patients. Dosing of insulin may depend on the patient's insulin sensitivity, which is reflected by the patient's total (basal and prandial) daily dose of insulin. Sliding-scale insulin regimens are commonly used[30–32]; however, they have been questioned in recent years.[5] Another approach to calculating the initial insulin dose is based on the "rule of 1800" (for rapid-acting insulin) or the "rule of 1500" (for regular insulin), which provides the expected decrease in blood glucose with each unit of insulin. The "rule of 1800" is more conservative than the 1500 rule. However, some authors have recommended the use of the "rule of 1500" for all surgical patients.[47] Thus, 1800 or 1500 is divided by total daily insulin dose to determine the expected decrease in blood glucose level with 1 unit of insulin. For example, if the patient's daily insulin requirement is 60 U, each unit of insulin would reduce the blood glucose level by 25 to 30 mg/dL (i.e., 1500/60 or 1800/60).

Should an Insulin-Naïve Patient Receive Insulin to Optimize Blood Glucose Levels?

There is insufficient evidence in the literature to guide insulin use in an insulin-naïve patient. There has been reluctance on the part of physicians to use insulin in patients with type 2 diabetes who take only oral antidiabetic medications because of concerns of hypoglycemia.[49] However, such reluctance may be misplaced because many of these patients eventually require insulin therapy in addition to an oral hypoglycemic drug as part of the natural progression of their disease. In fact, only a relatively low incidence of hypoglycemia has been reported in

patients who have been recently prescribed insulin because of the failure of oral hypoglycemic therapy.[25,26] Therefore, perioperative insulin therapy may be considered in this setting if the blood glucose levels are increased significantly (i.e., if there are concerns of severe dehydration, ketoacidosis, and hyperosmolar nonketotic states) and if the patient will be able to test his or her blood glucose levels at home (LoE category 2A).

What Are the Other Considerations Specific to Glycemic Control in Diabetic Outpatients?

When possible, diabetic patients should be scheduled as the first case of the day to minimize disruption to their routine and allow smooth and prompt return to their normal dosing regimen and meal plan. Patients should be asked to bring all their insulins with them to the facility and to travel with a suitable treatment such as clear juices for hypoglycemia that might occur in transit. Glucose tablets or gels are usually particulate in nature and therefore should be avoided in the preoperative period. Adequate preoperative hydration (i.e., consumption of water until 2 hours before surgery) and adequate intraoperative crystalloid administration (20 to 40 mL/kg bolus, assuming there are no contraindications such as history of congestive heart failure) should prevent postoperative dehydration.[50–52]

Aggressive nausea and vomiting prophylaxis and avoidance of factors that might increase postoperative nausea and vomiting (PONV) such as postoperative opioids should allow early resumption of oral intake.[6] Dexamethasone is a well-established antiemetic and is routinely used either alone or in combination with other antiemetics for the prevention of PONV.[6] The use of dexamethasone, even after a relatively modest single dose, has been demonstrated to transiently increase perioperative blood glucose levels.

Dexamethasone in a dose of 10 mg IV has been reported to increase blood glucose concentrations in diabetic and nondiabetic patients.[53,54] Hans et al.[55] prospectively investigated the change in perioperative blood glucose after dexamethasone 10 mg IV in type 2 diabetic patients who were treated exclusively with oral hypoglycemics and in nondiabetic patients. They found that blood glucose concentrations increased significantly over time (4 hours) and peaked at 2 hours in both groups. The magnitude of increase was around 20% from baseline and was comparable between the 2 groups. Maximum concentrations were higher in the diabetic group (8.97 ± 1.51 mmol/L) than in the nondiabetic group (7.86 ± 1.00 mmol/L). Of interest, 50% of the subjects underwent bariatric surgery, and the authors found that the body mass index and preoperative HbA1c values were determinant factors of perioperative blood glucose concentration.

In another study of bariatric surgery patients with impaired glucose tolerance, dexamethasone was associated with significantly increased postoperative blood glucose concentrations.[56] Overall, the increase in blood glucose levels after a single dose of dexamethasone 8 to 10 mg appears to be similar between diabetic and nondiabetic patients, and there is no evidence that this increase results in poor outcomes in either population. It is highly likely that the increase in blood glucose levels with dexamethasone 4

mg, which provides similar PONV prophylaxis as does 8 mg,[53] would be lower than that after dexamethasone 8 mg. Therefore, dexamethasone 4 mg can be used for PONV prophylaxis (LoE category 2A). Diabetic patients receiving dexamethasone should have appropriate monitoring of blood glucose levels (see the section on monitoring) and correction of hyperglycemia if necessary (LoE category 2A).

What Is the Optimal Perioperative Blood Glucose Monitoring?

Ambulatory surgical facilities taking care of diabetic patients must have glucose monitoring capabilities such as point-of-care monitors. Adequate monitoring of blood glucose levels is critical in maintaining patient safety and should facilitate insulin titration to achieve optimal blood glucose levels as well as allow for early detection of hypoglycemia. It has been suggested that blood glucose levels should be checked on the patient's arrival to the facility before surgery and before discharge home (LoE category 2A). Intraoperative blood glucose monitoring can be performed every 1 to 2 hours, depending upon the duration of procedure and type of insulin used. For example, intraoperative monitoring may not be necessary for procedures <2 hours. Similarly, because the peak effects with newer rapid-acting insulins occur within 90 minutes, blood glucose may be monitored in an hour. Obviously, more frequent measurements may be required for patients who have received intraoperative insulin and those with lower blood glucose levels.

In physiologically stable patients, point-of-care monitors correlate well with laboratory reference values.[1] However, point-of-care monitors tend to overestimate blood glucose values in comparison with laboratory readings during periods of hypoglycemia.[4,57] Use of a higher blood glucose level (e.g., <70 mg/dL) as an alert value for hypoglycemia (see the section on hypoglycemia) and more frequent monitoring should maintain patient safety. Furthermore, significantly low glucose levels should be corroborated with central laboratory tests.[4]

How Should We Identify and Manage Perioperative Hypoglycemia?

Hypoglycemia may cause functional brain failure, and if profound or prolonged, can lead to brain death.[58] Occurrence of hypoglycemia is of great concern during general anesthesia and sedation, because the symptoms of hypoglycemia are masked. Therefore, a high index of suspicion as well as planning for prevention, identification, and management of hypoglycemia in diabetic patients receiving sedation and general anesthesia is critical.

Preventive measures include identification of patients at risk for hypoglycemia and appropriate alterations in the preoperative antidiabetic therapy.[25,33] Increased vigilance is necessary in patients with aggressive glycemic therapy (low HbA1c or tight glycemic control), those with labile glycemic control, and those with a history of frequent hypoglycemia.[25,33] Notably, geriatric patients experience fewer hypoglycemic symptoms.[27] Use of peakless basal insulin analogs (instead of insulins with peak) and rapid-acting prandial insulin analogs (instead of regular insulin)

and use of continuous subcutaneous insulin infusion result in fewer incidences of hypoglycemia.[27,28,59]

Patients with long-standing type 2 diabetes are at a risk of developing hypoglycemia-associated autonomic failure because defective glucose counterregulation leads to impairment or even loss of the warning symptoms of hypoglycemia, also termed *hypoglycemia unawareness*.[25,60] Similarly, patients with poorly controlled type 2 diabetes may experience hypoglycemic symptoms at blood glucose levels that are usually considered normal.[25] Importantly, adequate perioperative monitoring of blood glucose levels as prescribed above should allow prevention and early diagnosis of hypoglycemia.

Diagnosis of hypoglycemia is based upon symptoms, blood glucose levels, or both. In an awake patient, hypoglycemia may cause sweating, palpitations, weakness, fatigue, confusion, and behavioral changes followed by seizure, loss of consciousness, brain damage, or death. Although there is some disagreement, a blood glucose level of <70 mg/dL is generally considered an alert value for hypoglycemia.[25] Use of this value as a trigger for therapy allows time for prevention of symptomatic hypoglycemia, which usually occurs at blood glucose levels of 45 to 55 mg/dL.[25]

In the symptomatic patient, the preferred method for treatment of hypoglycemia is consumption of 10 to 25 g of glucose, which is repeated until blood glucose increases and symptoms resolve. Clear liquids suitable for treating hypoglycemia include sugary drinks, sodas, electrolyte solutions, and fruit juices (e.g., 4 oz. apple juice). In patients with symptomatic hypoglycemia who are unable to ingest glucose and do not have IV access, subcutaneous glucagon 1 mg may be administered while attempts are made to obtain IV access. If IV access is established, an initial glucose dose of 20 to 50 mL (10 to 25 gm) dextrose 50% may be given.[61] Hyperglycemia after glucose administration can have significant detrimental effects, particularly in the presence of significant brain ischemia, and it should be avoided. Of note, the increase in blood glucose levels after oral or IV glucose administration is transient, and patients may require further, sustained glucose therapy after initial improvement in symptoms or blood glucose levels.

What Are the Discharge Considerations for Diabetic Outpatients?

In addition to achieving discharge criteria,[62] patients should be observed in an ambulatory facility until the possibility of hypoglycemia from perioperatively administered insulin is excluded. Many ambulatory patients are able to consume adequate oral intake to counteract potential hypoglycemia, but if not, they should be observed for an appropriate period of time after the last dose of insulin. The risk of hypoglycemia with subcutaneous rapid-acting insulin subsides within 1.5 hours, whereas that for subcutaneous regular insulin subsides in about 3 to 4 hours after the last dose is administered.[24,25]

What Advice Should We Give to Patients for Glucose Control After Discharge Home?

Patients need to receive clear and consistent instructions regarding plans for return to preoperative antidiabetic therapy and management of potential hypoglycemia. They should be instructed to check blood glucose levels frequently while fasting. Patients should carry hypoglycemia treatments while traveling to and from the surgical facility. While patients can resume the preoperative antidiabetic therapy once they are eating, they must be cautious with overlapping times of medication administration due to delayed dosing of morning medications. Resumption of antidiabetic therapy should be based on perioperative course and any treatments received. Because most oral hypoglycemics act on ingested food, these should be restarted once food intake is resumed. Patients should be advised that transition to daily preoperative antidiabetic regimens should be delayed if normal caloric intake is delayed.

What Are the Areas for Future Research?

This review has identified several areas for future research for which current data are insufficient or conflicting. There is a need for further large, adequately powered, well-designed randomized trials to assess all the clinical questions included in this review. In addition, there is a need to evaluate the impact of the recommendations provided in this consensus statement (e.g., preoperative continuation or discontinuation of oral hypoglycemics, risks and benefits of using rapid acting insulin to optimize perioperative blood glucose levels, and need for delaying discharge home after insulin administration).

Other questions that need to be addressed are as follows:

- Does scheduled time of the surgery (i.e., early vs. late) have any significant influence on outcomes, and if so, is there a patient subpopulation for which it does particularly?
- What is the impact of use of various preoperative regimens on short-term (e.g., morbidities and duration of recovery room, hospital stay and quality of recovery) and long-term (e.g., unplanned hospital admission, 30-day unexpected hospitalization, morbidity, and mortality) outcome in the ambulatory setting?
- What is the effect of preoperative insulin therapy on outcome after ambulatory surgery? Is there any benefit to aggressive preoperative glycemic control?
- Are there differences in optimal target blood glucose levels for high-risk outpatients versus low-risk outpatients?
- Are there differences in optimal blood glucose management in type 1 versus type 2 diabetes in the ambulatory setting?
- Are there differences in patient outcome between the various routes of administration of insulin?
- What is the optimal prophylactic antiemetic therapy in diabetic outpatients?
- Are there any predictors (e.g., blood glucose levels, HbA1c levels, and other comorbidities) that suggest avoidance of ambulatory surgery or need for overnight hospital admission?
- What is the impact of anesthetic technique (local/regional anesthesia, sedation/analgesia technique, general anesthesia) on blood glucose control? ▪

REFERENCES

1. Akhtar S, Barash PG, Inzucchi SE. Scientific principles and clinical implications of perioperative glucose regulation and control. Anesth Analg 2010;110:478–97

2. Griesdale DEG, de Souza RJ, van Dam RM, Heyland DK, Cook DJ, Malhotra A, Dhaliwal R, Henderson WR, Chittock DR, Finfer S, Talmor D. Intensive insulin therapy and mortality among critically ill patients: a meta-analysis including NICE-SUGAR study data. CMAJ 2009;180:821–7

3. Wiener RS, Wiener DC, Larson RJ. Benefits and risks of tight glucose control in critically ill adults: a meta-analysis. JAMA 2008;300:933–44

4. Polk HC Jr. Renewal of surgical quality and safety initiatives: a multispecialty challenge. Mayo Clin Proc 2006;81:345–52

5. Moghissi ES, Korytkowski MT, Dinardo M, Einhorn D, Hellman R, Hirsch IB, Inzucchi SE, Ismail-Beigi F, Kirkman MS, Umpierrez GE. Am Association of Clinical Endocrinologists and Am Diabetes Association consensus statement on inpatient glycemic control. Diabetes Care 2009;32:1119–31

6. Gan TJ, Meyer TA, Apfel CC, Chung F, Davis PJ, Habib AS, Hooper VD, Kovac AL, Kranke P, Myles P, Philip BK, Samsa G, Sessler DI, Temo J, Tramer MR, Vander Kolk C, Watcha M. Society for Ambulatory Anesthesia guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2007;105:1615–28

7. Higgins J, Green, S. (eds.). Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.0 [updated February 2008]. Available from wwwcochrane-handbookorg, 2008

8. Dalkey N, Helmer O. An experimental application of the Delphi method to the use of experts. Management Science 1963;9:458–67

9. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ, GRADE Working group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924–6

10. Guyatt GH, Oxman AD, Kunz R, Vist GE, Falck-Ytter Y, Schünemann HJ, GRADE Working group. What is "quality of evidence" and why is it important to clinicians? BMJ 2008;336:995–8

11. Guyatt GH, Oxman AD, Kunz R, Falck-Ytter Y, Vist GE, Liberati A, Schünemann HJ, GRADE Working group. Going from evidence to recommendations. BMJ 2008;336:1049–51

12. Belhoula M, Ciebiera JP, De La Chapelle A, Boisseau N, Coeurveille D, Raucoules-Aime M. Clonidine premedication improves metabolic control in type 2 diabetic patients during ophthalmic surgery. Br J Anaesth 2003;90:434–9

13. Christiansen CL, Schurizek BA, Malling B, Knudsen L, Alberti KG, Hermansen K. Insulin treatment of the insulin-dependent diabetic patient undergoing minor surgery. Continuous intravenous infusion compared with subcutaneous administration. Anaesthesia 1988;43:533–7

14. Gandhi GY, Murad MH, Flynn DN, Erwin PJ, Cavalcante AB, Bay Nielsen H, Capes SE, Thorlund K, Montori VM, Devereaux PJ. Effect of perioperative insulin infusion on surgical morbidity and mortality: systematic review and meta-analysis of randomized trials. Mayo Clin Proc 2008;83:418–30

15. Hemmerling TM, Schmid MC, Schmidt J, Kern S, Jacobi KE. Comparison of a continuous glucose–insulin–potassium infusion versus intermittent bolus application of insulin on perioperative glucose control and hormone status in insulin-treated type 2 diabetics. J Clin Anesth 2001;13:293–300

16. Malling B, Knudsen L, Christiansen CL, Schurizek BA, Alberti KGMM, Hermansen K. Insulin treatment in non-insulin dependent diabetic patients undergoing minor surgery. Diabetes, Nutrition and Metabolism—Clinical and Experimental 1989;2:125–31

17. Meyers EF, Alberts D, Gordon MO. Perioperative control of blood glucose in diabetic patients: a two-step protocol. Diabetes Care 1986;9:40–5

18. Parish M, Mahmoodpoor A, Sanaie S. Validity of fasting blood sugar on the day of surgery compared with the preinduction blood glucose level in type II diabetic patients. Pak J Med Sci 2007;23:202–5

19. Raucoules-Aime M, Ichai C, Roussel LJ, Romagnan MJ, Gastaud P, Dolisi C, Grimaud D. Comparison of two methods of i.v. insulin administration in the diabetic patient during the perioperative period. Br J Anaesth 1994;72:5–10

20. Raucoules-Aime M, Roussel LJ, Rossi D, Gastaud P, Dolisi C, Grimaud D. Effect of severity of surgery on metabolic control and insulin requirements in insulin-dependent diabetic patients. Br J Anaesth 1995;74:231–3

21. Thompson J, Husband DJ, Thai AC, Alberti KG. Metabolic changes in the non-insulin-dependent diabetic undergoing minor surgery: effect of glucose–insulin–potassium infusion. Br J Surg 1986;73:301–4

22. American Diabetes Association. Standards of medical care in diabetes—2009. Diabetes Care 2009;32:S13–61

23. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, Zinman B, American Diabetes Association, European Association for Study of Diabetes Consensus Committee. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2009;32:193–203

24. Mooradian AD, Bernbaum M, Albert SG. Narrative review: a rational approach to starting insulin therapy. Ann Intern Med 2006;145:125–34

25. Cryer PE, Axelrod L, Grossman AB, Heller SR, Montori VM, Seaquist ER, Service FJ, Endocrine Society. Evaluation and management of adult hypoglycemic disorders: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2009;94:709–28

26. Cryer PE. Preventing hypoglycaemia: what is the appropriate glucose alert value? Diabetologia 2009;52:35–7

27. Gough SC. A review of human and analogue insulin trials. Diabetes Res Clin Pract 2007;77:1–15

28. Hirsch IB. Insulin analogues. N Engl J Med 2005;352:174–83

29. Jacober SJ, Scism-Bacon L, Zagar AJ, IONW Study Investigators. A comparison of intensive mixture therapy with basal insulin therapy in insulin-naïve patients with type 2 diabetes receiving oral antidiabetes agents. Diabetes, Obesity, Metabolism 2006;8:448–55

30. Jacober SJ, Sowers JR. An update on perioperative management of diabetes. Arch Intern Med 1999;159:2405–11

31. Ahmed Z, Lockhart CH, Weiner M, Klingensmith G. Advances in diabetic management: implications for anesthesia. Anesth Analg 2005;100:666–9

32. Maynard G, O'Malley CW, Kirsh SR. Perioperative care of the geriatric patient with diabetes or hyperglycemia. Clin Geriatr Med 2008;24:649–65

33. Shorr RI, Ray WA, Daugherty JR, Griffin MR. Incidence and risk factors for serious hypoglycemia in older persons using insulin or sulfonylureas. Arch Intern Med 1997;157:1681–86

34. Van Staa T, Abenhaim L, Monette J. Rates of hypoglycemia in sulfonylurea users. J Clin Epidemiolog 1997;50:735–41

35. Bailey CJ, Day C. Fixed-dose single tablet antidiabetic combinations. Diabetes, Obesity and Metabolism 2009;11:527–33

36. Salpeter SR, Greyber E, Pasternak GA, Salpeter EE (posthumously). Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus. Cochrane Database Syst Rev 2010 Jan 20;:CD002967

37. Chan NN, Feher MD. Metformin and perioperative risk. Br J Anaesth 1999;83:540–1

38. De Heer J, Holtst JJ. Sulfonylurea compounds uncouple the glucose dependence of the insulinotropic effect of glucagon-like peptide. Diabetes 2007;56:438–43

39. Vann MA. Perioperative management of ambulatory surgical patients with diabetes mellitus. Curr Opin Anesthesiol 2009;22:718–24

40. Kao LS, Meeks D, Moyer VA, Lally KP. Peri-operative glycemic control regimens for preventing surgical site infections in adults. Cochrane Database of Systematic Reviews 2009;3:CD006806

41. Drange AS, Perkal MF, Kancir S, Concato J, Aslan M, Rosentahl RA. Long-term glycemic control and postoperative infectious complications. Arch Surg 2006;141:375–80

42. Korzon-Burakowska A, Hopkins D, Matyka K, Lomas J, Pernet A, Macdonald I, Amiel S. Effects of glycaemic control on protective responses against hypoglycaemia in type 2 diabetes. Diabetes Care 1998;21:283–90

43. Amiel SA, Tamborlane W, Simonson DC, Sherwin RS. Defective glucose counterregulation after strict glycaemic control of insulin-dependent diabetes mellitus. N Engl J Med 1987;316:1376–83

44. Spyer G, Hattersley AT, MacDonald IA, Amiel S, MacLeod KM. Hypoglycaemic counter-regulation at normal blood glucose concentrations in patients with well controlled type-2 diabetes. Lancet 2000;356:1970–4

45. Monnier L, Mas E, Ginet C, Michel F, Villon L, Cristol JP, Colette C. Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. JAMA 2006;295:1681–7

46. Egi, M, Bellomo R, Stachowski E, French CJ, Hart G. Variability of blood glucose concentration and short-term mortality in critically ill patients. Anesthesiology 2006;105:244–52

47. Umpierrez GE, Latif K, Stoever J, Cuervo R, Park L, Freire AX, Kitabchi AE. Efficacy of subcutaneous insulin lispro versus continuous intravenous regular insulin for the treatment of diabetic ketoacidosis. Am J Med 2004;117:291–6

48. Umpierrez GE, Latif KA, Cuervo R, Karabell A, Freire AX, Kitabchi AE. Treatment of diabetic ketoacidosis with subcutaneous insulin aspart. Diabetes Care 2004;27:1873–8

49. Hayes RP, Fitzgerald JT, Jacober SJ. Primary care physician beliefs about insulin initiation in patients with type 2 diabetes. Int J Clin Prac 2008;62:860–8

50. Yogendran S, Buvenandran A, Cheng DCH, Chung F. A prospective randomized double-blinded study of the effect of intravenous fluid therapy on adverse outcomes on outpatient surgery. Anesth Analg 1995;80:682–6

51. Holte K, Klarskov B, Christensen DS, Lund C, Nielsen KG, Bie P, Kehlet H. Liberal versus restrictive fluid administration to improve recovery after laparoscopic cholecystectomy: a randomized, double-blind study. Ann Surg 2004;240:892–9

52. Brandstrup B. Fluid therapy for the surgical patient. Best Pract Res Clin Anaesthesiol 2006;20:265–83

53. Lukins MB, Manninen PH. Hyperglycemia in patients administered dexamethasone for craniotomy. Anesth Analg 2005;100:1129–33

54. Pasternak JJ, McGregor DG, Lanier WL. Effect of single-dose dexamethasone on blood glucose concentration in patients undergoing craniotomy. J Neurosurg Anesthesiol 2004;16:122–5

55. Hans P, Vanthuyne A, Dewandre PY, Brichant JF, Bonhomme V. Blood glucose concentration profile after 10 mg dexamethasone in non-diabetic and type 2 diabetic patients undergoing abdominal surgery. Br J Anaesth 2006;97:164–70

56. Nazar CE, Lacassie HJ, Lopez RA, Munoz HR. Dexamethasone for postoperative nausea and vomiting prophylaxis: effect on glycaemia in obese patients with impaired glucose tolerance. Eur J Anaesthesiol 2009;26:318–21

57. Kanji S, Buffie J, Hutton B, Bunting PS, Singh A, McDonald K, Fergusson D, McIntyre LA, Hebert PC. Reliability of point-of-care testing for glucose measurement in critically ill adults. Crit Care Med 2005;33:2778–85

58. Cryer PE. Hypoglycemia, functional brain failure, and brain death. J Clin Invest 2007;117:868–70

59. Horvath K, Jeitler K, Berghold A, Ebrahim SH, Cratzer TW, Plank J, Kaiser T, Pieber TR, Siebenhofer A. Long-acting insulin analogues versus NPH insulin (human isophane insulin) for type 2 diabetes mellitus. Cochrane Database Syst Rev:CD005613

60. Segel SA, Paramore DS, Cryer PE. Hypoglycemia-associated autonomic failure in advanced type 2 diabetes. Diabetes 2002;51:724–33

61. Krinsley JS, Grover A. Severe hypoglycemia in critically ill patients. Risk factors and outcomes. Crit Care Med 2007;35:2262–7

62. Practice guidelines for postanesthesia care. A report by the American Society of Anesthesiologists Task Force on postanesthesia care. Anesthesiology 2002;96:742–52