PERI-OPERATIVE DIABETES MANAGEMENT GUIDELINES

AUSTRALIAN DIABETES SOCIETY

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FOREWORD

People with diabetes are more likely to require admission to hospital (for conditions other than their diabetes) and are more likely to undergo surgery or other procedures that may potentially disrupt their glycaemic control. The metabolic impact of surgery, fasting and interruptions to usual therapy contribute to poor glycaemic control, which in turn is a significant factor contributing to the increased mortality, morbidity and length of hospital stay in patients with diabetes undergoing surgery. Minimising such disruptions has the potential to reduce the risk of such adverse outcomes.

Pre- as well as peri-operative management of diabetes is often provided in an ad-hoc fashion by staff with limited expertise in this area. Early discharge from hospital and the increasing use of day-only procedures have resulted in an increased burden on the patient and their carers for the management of their diabetes for which they may be ill-prepared and without adequate medical support.

These guidelines, developed by an ADS working group of Vincent Wong, Glynis Ross, Jennifer Wong and David Chipps (chair), are primarily intended to provide assistance for those practitioners whose primary focus is not diabetes or do not have the support of local diabetes expertise, in their management of patients with diabetes undergoing surgical procedures. Evidence supporting much of the advice contained in these guidelines is largely lacking, and indeed may never eventuate. They therefore represent a consensus of the opinions of the authors. They are not intended to replace protocols that may have been developed by other diabetes experts that are appropriate for their specific hospital circumstances. As experience continues to be gained, diabetes treatment options expand and surgical procedures advance, modifications to the advice contained therein may need to be made. By improving glycaemic control in the peri-operative period, it is hoped to reduce the potential for an adverse outcome for the patient with diabetes who has undergone a surgical or investigative procedure.

SUMMARY

- Prevention of hyperglycaemia reduces the risk of adverse outcomes post-operatively for people with diabetes.
- Elective surgery should be postponed if possible if glycaemic control is poor.
- All patients treated with insulin should be managed in the same way, irrespective of the type of diabetes.
- For the purposes of these guidelines, all day-only surgery is regarded as minor, whereas surgery requiring over-night admission post-operatively is defined as major.
- Associated complications of diabetes may affect the outcome of, as well as be affected by the surgery.
- It is essential to ensure that patients with diabetes undergoing day-only surgery are capable of and have written guidelines about managing their diabetes post-operatively, and that they have access to professional advice if glycaemic control deteriorates.
- Each surgical facility should have protocols to ensure that diabetes control is not compromised by the surgical procedure, including the ability to commence an insulin-glucose infusion if necessary.
- The target blood glucose range post-operatively should generally be 5-10 mmol/L, although this can /should be modified in specific settings, e.g. ICU.
- Surgery for patients with diabetes should ideally be performed in the morning, as this is least disruptive to their usual diabetes management routine, and is least disruptive to their glycaemic control.
- It is important to ensure that the insulin-treated patient does not become insulin deficient and therefore hyperglycaemic at a time of metabolic stress, yet at the same time, ensure that the risk of hypoglycaemia is minimised at a time when the oral consumption of carbohydrate is restricted.
- An insulin-glucose infusion is the best way of maintaining euglycaemia post-operatively, especially in those previously treated with insulin, poorly controlled prior to admission, receiving more than one type of oral anti-hyperglycaemic medication, or who are not capable of resuming their usual diet and treatment. Traditional "sliding scale insulin" is usually ineffective and a "basal-bolus" insulin regimen is preferable once the patient has resumed eating when post-operative insulin requirements are unknown.
- Insulin-treated patients undergoing major surgery on a morning operating list should commence an insulin-glucose infusion either prior to or at the time of induction of anaesthesia (or by 1000hrs at the latest) and the infusion should be continued for 24 hours post-operatively or until the patient is eating adequately.

- Insulin-treated patients undergoing major surgery on an afternoon operating list should receive a modified dose of insulin (see specific instructions) with an early breakfast, be admitted early to the pre-operative ward for blood glucose monitoring, and commence an insulin-glucose infusion prior to the induction of anaesthesia.

- Insulin-treated patients undergoing minor surgery on a morning operating list may be able to delay their morning insulin injection and breakfast until after the procedure, provided that they are first on the list, the procedure is short, and they will have recovered and be capable of eating by 1000hrs. Otherwise, a modified dose of insulin can be given in the morning (see specific instructions), with quick-acting insulin given before the first meal post-operatively.

- Insulin-treated patients undergoing minor surgery on an afternoon list should receive a modified dose of insulin in the morning (see specific instructions), some quick acting insulin before the first post-operative meal.

- Non-insulin treated patients receiving more than one type of oral anti-hyperglycaemic medication and undergoing major surgery should be managed with an insulin-glucose infusion for the first 24hrs post-operatively.

- Metformin does not need to be withdrawn prior to minor surgery, but should be replaced by an insulin-glucose infusion for the first 24hrs following major surgery.

- Advice is also provided for patients undergoing bowel investigations and radiological and other imaging procedures that involve a period of fasting or the administration of radio-contrast.

INTRODUCTION

Patients with diabetes have a higher incidence of morbidity and mortality following surgery [Axelrod et al. 2002; Babineau and Bothe 1995; Juul et al. 2004a; Sandler et al. 1986; Virkkunen et al. 2004] and have an increased length of stay in hospital. However, diabetes is often managed in an ad-hoc fashion by those with limited expertise in this area. The aim of this document is to provide guidance for the management of patients with diabetes during the peri-operative period. Whilst modern anaesthetic and surgical techniques have reduced the metabolic impact of surgery, early discharge from hospital and the increasing use of day-only procedures places greater responsibility on the person with diabetes and their carers for the management of their diabetes in an unfamiliar situation, for which they may be ill-prepared and when medical assistance may not be readily available.

Evidence supporting much of the advice given in these guidelines is largely lacking and for many of the situations covered in this document may never eventuate. Hence, these guidelines represent a consensus of the opinions of the authors, and are primarily intended to assist those practitioners

whose primary focus is not diabetes in their management of patients with diabetes undergoing surgical procedures, or who do not have the support of local diabetes expertise. When such expertise is available, guidelines reflecting local circumstances or addressing specific surgical situations may supplant the more general advice contained in these guidelines.

RATIONALE FOR MAINTENANCE OF EUGLYCAEMIA

- Poor peri-operative glycaemic control increases the risk of adverse outcomes.

Hyperglycaemia is associated with an increased risk of adverse outcomes in hospitalized patients, with both medical and surgical conditions, irrespective of whether the patient is known to have diabetes or not [Capes et al. 2000; Capes et al. 2001; Umpierrez et al. 2002]. For the surgical patient, there is a strong correlation between peri-operative hyperglycaemia and increased complications following surgery, especially nosocomial infection [Golden et al. 1999; Guvener et al. 2002; McAlister et al. 2003; Pomposelli et al. 1998] with the blood glucose control on the first post-operative day having a major influence [Zerr et al, 1997]. Pre-operative glycaemic control also influences the risk of post-operative wound infection, with a recent study suggesting a HbA1c $\geq$ 7% more than doubles this risk [Dronge et al, 2006].

- Treatment of post-operative hyperglycaemia reduces the risk of adverse outcomes.

Prevention of hyperglycaemia reduces the risk of post-operative complications of cardiac surgery [Zerr et al, 1997, Furnary et al, 2003, Lazar et al, 2004] as well as morbidity and mortality in patients in ICU [van den Berghe et al, 2001]

Whilst modern anaesthetic and surgical techniques have reduced the metabolic impact of surgery, it is reasonable to assume that the benefits of good glycaemic control extend beyond the cardio-thoracic unit and the ICU and are applicable to all patients with diabetes undergoing a surgical procedure, although the target blood glucose levels may need to be modified according to specific situations.

More detailed discussion concerning peri-operative glycaemic control can be found in the "ACE / ADA Consensus Statement on Inpatient Diabetes and Glycemic Control" in Diabetes Care 2006: 29 (8) 1955-1962, and in the review by Lipshutz and Gropper, (2009).

TARGETS FOR THERAPY

- Postpone elective surgery if possible if glycaemic control is poor (HbA1c $\geq$ 9%).
- BGL should be kept between 5 – 10mmol/l during the peri-operative period
- For critically ill patients who require admission to the intensive care unit post-operatively, a "tighter" BGL target (e.g 4.4-6.1 mmol/L) may not convey any greater benefit.

- Hypoglycaemia must be avoided.

Whilst a HbA1c ≥ 7% (which corresponds to a mean plasma glucose level of ≥8.4 mmol/L) is associated with an increased risk of post-operative wound infection, it would be unrealistic to recommend that elective surgery be postponed in all such patients. A pre-operative HbA1c target of < 8% (mean plasma glucose of <10.2 mmol/L) in elective surgical patients would seem to be more appropriate. It is therefore not unreasonable to suggest that elective surgery be postponed if HbA1c ≥ 9% (mean blood glucose of ≥11.9 mmol/L).

The optimal target blood glucose range in the post-operative period may be dependent on the clinical context. In the ICU, where closer supervision is also possible, maintaining blood glucose levels between 4.4-6.1 mmol/L has been shown to significantly reduce morbidity and mortality in some studies (van den Berghe et al, 2001, 2006), yet increase mortality in others (The NICE-SUGAR Study Investigators, 2009). Until more analyses are conducted and a consensus on target BGLs in the ICU is reached, it seems reasonable to recommend a blood glucose target of at least 5-10 mmol/L in the ICU. Following coronary artery bypass surgery, maintaining blood glucose levels between 6.9-11.1 mmol/L results in reduced post-operative morbidity and mortality (Lazar et al, 2004), but there is a lack of evidence in favour of a specific post-operative blood glucose range in other surgical settings. Nonetheless, given the evidence for impaired neutrophil function with blood glucose > 11 mmol/L, it seems reasonable to recommend that blood glucose levels also be maintained between 5-10 mmol/L post-operatively in the non-ICU setting. However, it is also important to ensure that hypoglycaemia is avoided.

In order to ensure that glycaemic control is maintained post-operatively, each surgical facility must have the ability to monitor blood glucose levels at the patient's bed-side, be able to administer insulin-glucose infusions safely and effectively and have policies in place governing the management of diabetes in the post-operative period, including the involvement of or consultation with specialised diabetes services when necessary.

DEFINITIONS

- All patients with diabetes treated with insulin should be managed in the same way, irrespective of whether they have type 1 or type 2 diabetes mellitus.

- Minor surgery is defined as all day-only procedures, while major surgery includes all procedures that require at least an overnight admission.

The distinction between type 1 and type 2 diabetes can be difficult at times, especially with respect to type 2 diabetes of long duration. Patients with type 1 diabetes are prone to develop diabetic ketosis or ketoacidosis within hours if insulin is withdrawn or omitted, especially at times of physiological stress (such as surgery) when counter-regulatory hormone production is increased. Patients with type 2 diabetes may also develop diabetic ketoacidosis if sufficiently physiologically stressed and sufficiently insulin deficient (such patients usually have had diabetes for >10 years and require multiple injections of insulin for glycaemic control). Therefore, the more insulin deficient the patient, the greater the metabolic impact of surgery. Post-operative

hyperglycaemia should be anticipated and prevented in such patients undergoing major surgery. It is therefore easier to assume that all patients treated with insulin are insulin deficient and are managed accordingly. Thus all patients with diabetes treated with insulin should be treated with the same protocol (with the exception of those treated with a single night-time injection of intermediate or long-acting insulin, in combination with oral therapy). If such patients are usually cared for by a diabetes specialist, then it would be preferable if the expertise of the diabetes specialist was utilised in the peri-operative management of the patients' diabetes.

The definition of "major" or "minor" surgery is also arbitrary. For the purpose of these guidelines, any day-only procedure is defined as "minor", and all surgery that requires at least an overnight stay is considered to be "major". In the following sections, short-acting insulin includes regular insulin, Lispro, Aspart and Glulisine. Intermediate-acting insulin includes Isophane and Detemir, and long-acting insulin includes Glargine.

PRE-OPERATIVE EVALUATION

- Determine the type of diabetes and its management.
- Ensure that the patient's diabetes is well controlled.
- Ensure that the patient is capable of managing their diabetes after discharge from hospital.
- Consider the presence of complications of diabetes that might be adversely affected by or that might adversely impact upon the outcome of the proposed procedure.

Whilst many of these aspects are dealt with in other sections of this document, it is worthwhile emphasising the importance of pre-operative glycaemic control in influencing the risk of an adverse outcome of the procedure, and surgery should ideally only be performed if glycaemic control is stable (HbA1c < 8%, and in the absence of significant hypo- or hyperglycaemia).

The patients' ability to management their diabetes after discharge does not just depend upon their cognitive capacity but may also be affected by the operation itself, such as the inability to self-administer their insulin or test their own blood glucose level after hand or wrist surgery (such as carpal tunnel decompression).

Complications of diabetes may alter the outcomes of surgery and determine the peri-operative support required, including the feasibility of day-only surgery. Beginning with pre-operative fasting, the presence of diabetic gastroparesis may result in incomplete emptying of gastric contents, thereby either increasing the risk of aspiration at induction of anaesthesia or prolonging the duration of the fast. Gastroparesis may also result in persistent nausea or vomiting post-operatively with consequent delayed resumption of oral intake. Patients with gastroparesis are therefore not usually suitable for day-only surgery which requires general anaesthesia.

Patients with autonomic neuropathy may also have impaired cardiovascular reflexes resulting in hypotension at the induction of anaesthesia, as well as an impaired respiratory drive post-

operatively, and the anaesthetist should be therefore be informed if autonomic neuropathy is present.

Surgery may also precipitate myocardial ischaemia. The presence of significant coronary artery disease may not always result in typical symptoms of ischaemic heart disease. Silent myocardial ischaemia may be present in up to 20% of patients with diabetes, especially those with macrovascular disease elsewhere, with microalbuminuria or with 2 or more additional cardiovascular risk factors. Such patients should undergo cardiac evaluation prior to major surgery.

The routine use of beta-blockers peri-operatively for patients with diabetes undergoing non-cardiac surgery does not reduce cardiac events, and is therefore not recommended (Juul et al, 2004b).

For patients with diabetic nephropathy, it is important to avoid dehydration and nephrotoxic drugs, whilst the dose of other medications may need to be altered because of changes in drug clearance.

GENERAL PRINCIPLES

- Diabetes should be well controlled prior to elective surgery.
- Avoid insulin deficiency, and anticipate increased insulin requirements.
- The patient's diabetes care provider should be involved in the management of their patients' diabetes peri-operatively.
- Patients must be given clear written instructions concerning the management of their diabetes both pre- and post-operatively (including medication adjustments) prior to surgery.
- Patients must not drive themselves to the hospital on the day of the procedure.
- Patients with diabetes should be on the morning list, preferably first on the list.
- These guidelines may need to be individually modified depending on the patient's circumstances.

It is important that advice concerning diabetes management be provided by someone who is familiar with its complexities. To this end, the patient's usual diabetes care provider should be informed of the patient's impending surgery or procedure. Clear and simple written instructions must be given to patients regarding any required adjustment to their medications prior to surgery. Blood glucose monitoring (at least 3 – 4 times per day) should be performed frequently for a few days prior to the surgery. Patients should ensure they are well hydrated before the procedure. Due to the possibility of hypoglycaemia whilst fasting, patients should not drive themselves to the hospital on the day of surgery. They should bring their diabetes medications with them to the hospital to ensure accurate identification of the type of insulin or oral anti-hyperglycaemic

medications (AHG) by medical and nursing staff (given the many similar names of different types of diabetes treatments) and to facilitate resumption of the patient's usual therapy post-operatively. Patients with diabetes should ideally be first on a morning operating list, as this minimises disruption of the patient's usual routine and their glycaemic control. Throughout the intra-operative period as well as in the recovery ward, BGLs should be checked frequently, preferably hourly. Following discharge from hospital, reduced oral intake, post-operative infection or reduced mobility can result in glycaemic instability. Therefore, patients (and their carers) should have access to a contact person (the patient's diabetes care provider or the local diabetes centre) if they need assistance with their post-operative diabetes management.

The duration of fasting prior to surgery is often determined by the surgeon and anaesthetist, but is usually at least 6 hours for solids. For patients who are on the morning list, fasting conveniently starts at midnight the day before surgery. For patients with gastroparesis, a more prolonged fasting period is required. However, prolonged fasting increases catabolism and promotes insulin resistance, and such patients may benefit from commencing an insulin-glucose infusion pre-operatively whilst fasting.

The following recommendations are intended to provide guidelines for the management of diabetes during the peri-operative period. They may need to be modified in individual circumstances. Diabetes management is becoming more complex and the therapeutic options available are greater. It is not possible therefore to provide guidance for each and every possible treatment regimen and these guidelines therefore apply to the more common modes of diabetes treatments available.

PATIENTS WHO REQUIRE INSULIN THERAPY

This group includes patients with type 1 diabetes or patients with type 2 diabetes who require day time insulin injections. The more commonly used insulin regimens include:

- the "basal-bolus" regimen (short-acting insulin before each of the 3 main meals in the day, and intermediate- or long-acting insulin either before bed, twice daily or in the morning [Glargine]);
- twice daily or thrice daily pre-mixed insulin, and;
- a combination of short-and intermediate-acting insulin in the morning and evening.

Some patients receiving insulin may also take oral AHG.

For those patients whose insulin regimen is not discussed here, advice from their diabetes care provider should be sought.

Morning List

Patients should take their usual dose of insulin (as well as oral AHG) on the day prior to surgery, and fasting usually begins at midnight**.** Patients should be allocated first on the list if possible.

Major Surgery

- Maintain the usual insulin doses and diet the day before, and fast from midnight.
- Omit usual morning insulin (and AHG).
- Commence an insulin-glucose infusion prior to induction of anaesthesia (or by 1000hrs at the latest).
- Measure BGL at least hourly during the intra-operative period.
- Continue the insulin-glucose infusion for at least 24 hours post-operatively **and** until the patient is capable of resuming an adequate oral intake.

As indicated previously, "major surgery" is defined, for the purposes of these guidelines, as any surgical procedure that requires an overnight admission to hospital. Such surgery obviously therefore includes cardiothoracic surgery, some orthopaedic and neurosurgical procedures, intra-abdominal surgery such as cholecystectomy, laparotomy and if duration of surgery is >4 hours.

On the morning of surgery, the morning dose of insulin and oral AHG should be omitted. An insulin-glucose (I-G) infusion (using the protocol specific to the institution) should be commenced prior to the induction of anaesthesia. The I-G infusion should commence by 1000hrs in order to avoid insulin deficiency and consequent hyperglycaemia should surgery be delayed. Following the procedure, the I-G infusion should be continued for at least 24hrs post-operatively **and** until they have resumed an adequate oral intake.

In patients receiving an evening injection of Lantus insulin, given its prolonged duration of action, the initial insulin infusion rate should be reduced by 50% for at least the first 2 hours of the I-G infusion and the rate then adjusted according to the BGL. Should the pre-operative BGL be ≥8 mmol/L however, then the insulin infusion should be commenced at the usual rate. For patients receiving a morning injection of Lantus insulin, then the insulin infusion should be commenced at the usual rate.

Minor Surgery

- Delay the usual morning dose of insulin **provided that the procedure is completed and the patient is ready to eat by 1000hrs**. The patient can then have a late breakfast after the usual dose of insulin is given.
- For later procedures, give a reduced dose of insulin in the morning in the form of intermediate or long-acting insulin if possible.
- If the BGL remains elevated (>10mmol/l), an I-G infusion should be commenced.

For minor surgery, ie day-only procedures, the duration of surgery is short, the impact of the surgery on glycaemic control is minimal, recovery is quick, and resumption of the patient's usual diet and routine occurs within a short period of time. Insulin management is dependent on the timing and duration of the procedure and the resumption of the patient's usual diet.

For minor procedures that will be completed and the patient have recovered and be capable of resuming their usual diet by 1000hrs, then the patient's usual insulin and any oral AHGs can be withheld until after the procedure and the usual dose given prior to a delayed breakfast. However, if the procedure is delayed or prolonged or the patient is unable to resume eating by 1000hrs, then an I-G infusion must be commenced, as these patients will not have received any insulin prior to the procedure and may become significantly hyperglycaemic and/or ketotic. An I-G infusion will also be required if the BGL exceeds 10 mmol/L.

For procedures that will not be completed and the patient will not be capable of resuming their usual diet by 1000hrs, then a modified dose of insulin is usually given in the morning before surgery, in order to ensure that the patient does not become insulin deficient. This requires an understanding of the pharmacokinetics of the various subcutaneous insulin preparations available. For the patient receiving premixed insulin, this may preferably be administered on arrival at the pre-operative ward to avoid the occurrence of hypoglycaemia on the way to hospital. Patients should still omit their oral dose of AHG. Insulin dose modifications are detailed on the Instruction sheet (Figure 1). The general principle is to give half the usual day time insulin dose using intermediate- (Detemir, Isophane) or long-acting (Glargine) insulin, and try to avoid short-acting insulin (such as regular insulin, Lispro, Aspart, Glulisine). Patients receiving pre-mixed insulin twice a day can administer half of the usual morning dose early in the morning. Due to the short-acting component of the pre-mixed insulin, there is a risk of mid morning hypoglycaemia when patients are fasted. Therefore BGLs must be monitored regularly (e.g. 2nd hourly) throughout the morning, and if the BGL is less than 4.0mmol/L, glucose should be given intravenously.

Following the procedure, for those who are well enough to have lunch, a small amount (half of the usual dose) of short-acting insulin can be administered before their lunch. It is therefore important to ensure that short-acting insulin is available in the operating suite for administration to patients who may not normally administer this insulin (e.g. those receiving pre-mixed insulins). The patients should then resume their usual insulin (plus oral AHGs) and diet in the evening.

If patients have poorly controlled diabetes or have unstable BGLs during the few days prior to surgery, an I-G infusion should be used peri-operatively even for minor operations.

Afternoon List

Afternoon procedures are not ideal for insulin-treated patients as they are more disruptive to their glycaemic control. Patients usually commence fasting from 0600hrs (or sometimes 0800hrs) for the procedure after an early light breakfast. It is therefore necessary to provide a dose of insulin capable of both preventing hyperglycaemia as well as avoiding hypoglycaemia at a time when the patient is not able to consume oral carbohydrate to treat hypoglycaemia should it occur. If glycaemic control is unstable, then admit earlier and use an insulin glucose infusion.

Major Surgery

- Give a reduced dose of insulin before early breakfast in the morning.
- Patients should arrive at the facility by 0900hrs and BGLs should be monitored closely in the pre-operative ward.

- Commence an insulin-glucose infusion before induction of anaesthesia.

The recommendations for insulin medications are outlined in Figure 1. In principle, patients can have a small dose of short acting insulin before their light breakfast in the morning, together with half of the usual day-time insulin dose in the form of intermediate- or long-acting insulin. An I-G infusion should be commenced before the induction of anaesthesia for all patients undergoing major surgery and should be continued at least overnight, but preferably for the first 24hrs post-operatively and until meals can be tolerated when the usual subcutaneous insulin regimen can be resumed.

As the usual mid-morning snack will be omitted on the day of surgery, mid-morning hypoglycaemia may occur (especially those who use pre-mixed insulins or regular insulin as their short-acting insulin). Therefore, BGLs should be monitored second hourly following the morning insulin dose, and the patient should be advised to not drive on the day of the procedure. Patients with insulin-treated diabetes should be admitted to the pre-operative ward by 0900hrs even if they are on the afternoon list, for BGL monitoring, and intravenous glucose administration if necessary.

Patients receiving a combination of oral AHG and bed-time intermediate- or long-acting insulin (such as Lantus) only can take their usual medications including the night-time intermediate-acting insulin on the day before the procedure. If the fasting BGL has been relatively low (consistently less than 5.0mmol/l), the bed-time intermediate- or long-acting insulin dose can be reduced by 10% on the night before the procedure. Oral AHGs should be omitted on the morning of surgery. This group of patients will also require an I-G infusion to be commenced pre-operatively and are likely to require additional day-time (pre-meal) insulin post-operatively.

Minor Surgery

- Pre-operative insulin adjustments similar to that for major surgery in the afternoon.
- An insulin-glucose infusion may be necessary if pre-operative insulin adjustments result in hyperglycaemia.
- Overnight admission may be necessary for those with glycaemic instability or who are unable to resume their usual diet before discharge

Prior to minor surgery, insulin doses should be modified as previously outlined for major surgery. The patients' BGLs should be monitored closely throughout the peri-operative period, and an I-G infusion should be commenced if the adjustments to the morning dose of insulin result in hyperglycaemia (≥10 mmol/L) if the duration of surgery is prolonged or if they are unable to resume their usual diet. The usual subcutaneous evening dose of insulin should be resumed if they can tolerate an adequate oral intake. It is important to ensure that the patient and their carer are capable of managing the patient's diabetes after discharge. If glycaemic control becomes erratic during or following the procedure, the patient should be admitted overnight for observation and/or stabilization. Patients who are unable to eat should be commenced on an I-G infusion and admitted overnight for observation.

Insulin-Glucose Infusion

- An insulin-glucose infusion is the best way to maintain normoglycaemia, and each institution should have their own infusion protocol.

- Adequate training of staff is essential to ensure the proper implementation of the protocol

An I-G infusion is the most effective means of maintaining tight glycaemic control without causing hypoglycaemia during the peri-operative period. Each institution should have their own infusion protocol, and all require frequent BGL monitoring (hourly or second hourly at least). For most I-G infusion protocols, the insulin infusion rate is titrated according to the BGL in order to achieve a target BGL range (eg 5-10 mmol/L), while the glucose infusion rate is kept constant. This allows more precise glycaemic control. An example of an I-G infusion protocol can be found in the following website: http://www.joslin.org/Files/Inpatient_Guideline_final_4-30-07.pdf but all the major hospitals within Australia will have their own versions and a national insulin prescribing and monitoring chart, incorporating insulin-glucose infusion guidelines may shortly become available. If the initial blood glucose level is elevated (eg ≥15 mmol/L), then the glucose infusion should not be commenced until the blood glucose has improved. Otherwise, insulin must not be infused without a concomitant glucose infusion, in view of the risk of hypoglycaemia. Continuing education of the medical and nursing staff is most important in ensuring correct implementation of the I-G infusion guidelines and achievement of glycaemic targets.

Subcutaneous Insulin Infusion Pumps

These pumps can be used for minor procedures but are not appropriate for major surgery.

- The continuation of the insulin pump during the surgery should be discussed with the proceduralist and anaesthetist.

An increasing number of patients with type 1 diabetes use subcutaneous insulin infusion pumps. For minor or day-only surgery, the pump can be continued at the usual basal insulin infusion rate, but this must be discussed with the anaesthetist in advance. BGLs must be monitored hourly during the procedure. For major surgery, due to potential intra-operative fluctuations in haemodynamic status, subcutaneous absorption of insulin may vary, and counterregulatory hormone release may increase insulin requirements. Therefore, as patients will also not be able to manage the pump themselves during and immediately after surgery, an I-G infusion should be used instead. [Marks 2003].

PATIENTS WHO ARE NOT INSULIN REQUIRING

Patients on Diet Alone

- BGL monitoring should be performed more frequently during the peri-operative period.

For patients whose diabetes is maintained on diet alone and who are well controlled (HbA1c < 6.5%), no specific therapy is required, but more frequent BGL monitoring during the peri-operative period is recommended. During the procedure, BGLs should be checked hourly. If the

BGL remains above 10mmol/L in the pre- or peri-operative period, an I-G infusion should be commenced and continued until they resume eating. If the patient does not become hyperglycaemic following surgery, the patients' BGL should be monitored every 4 – 6 hours until they resume their usual meals. Patients who are hyperglycaemic peri- or post-operatively may require supplemental insulin and/or the initiation of specific AHG.

Patients on Oral AHG Medication (without insulin)

Major Surgery

- Stop AHG medication on the day of surgery.
- Restart AHG medication when patients are able to resume normal meals (except possibly metformin – see section I.3, and thiazolidinediones following cardiac surgery).
- Commence an I-G infusion if the BGL >10 mmol/L; if surgery is prolonged and complicated; or if the patient is usually treated with more than one oral AHG agent.
- Subcutaneous insulin may be required post-operatively.

Patients receiving AHG medications (metformin, sulphonylureas, repaglinide, acarbose, glitazones and DPP IV Inhibitors) as well as GLP-1 agonists such as Xenatide can continue their diabetes medications on the day prior to surgery. However, these should be omitted on the morning of surgery, irrespective of whether the patients are on the morning or afternoon list. Once they resume their meals, AHG medication can be restarted, with the possible exception of metformin (see section I.3) and the thiazolidinediones following cardiac surgery (given their risk of precipitating cardiac failure in patients with significant cardiac disease). If an AHG is withdrawn in the post-operative period, then glycaemic control will deteriorate unless alternative treatment strategies are implemented.

The metabolic impact of major surgery is greater in those patients who are more insulin deficient. In type 2 diabetes, insulin deficiency progressively increases with increasing duration of diabetes and is reflected in the number of oral AHG medications required to control hyperglycaemia. Therefore, patients receiving more than one oral AHG agent undergoing major surgery should be managed peri-operatively with an I-G infusion. An I-G infusion should also be commenced if BGLs are persistently above 10mmol/l, in those who had suboptimal pre-operative glycaemic control, or if the procedure is prolonged and/or complicated. Such patients are also likely to require subcutaneous insulin in the post-operative period.

Minor Surgery

- Peri-operative management is similar to that for major surgery.

Diabetes management guidelines for patients receiving oral AHG therapy (and GLP-1 agonists) undergoing minor surgery are similar to those for patients undergoing major surgery. The patient's AHG medication should be omitted on the morning of surgery. BGLs should be monitored before, during and after surgery, and patients can resume their AHG medication with dinner that evening. Patients receiving more than one AHG agent do not routinely require an I-G

infusion for minor surgery, although, an I-G infusion is still necessary if surgery is unexpectedly prolonged or if the patients' BGLs become erratic.

Metformin

Metformin and Surgery

- Metformin does not worsen renal function.
- For major surgery, metformin should be stopped on the day of surgery and recommenced if serum creatinine level does not deteriorate post-operatively.
- Prolonged cessation of metformin will result in deterioration of glycaemic control and additional anti-hyperglycaemic treatment will be required.
- Metformin need not be stopped for minor surgery.

Metformin does not worsen renal function. However, in patients with renal impairment, Metformin is associated with an increased risk of lactic acidosis particularly in situations where lactate production is also increased. The incidence of Metformin-associated lactic acidosis is 0.03 per 1000 patient years, but, mortality can be as high as 50% [Bailey and Turner 1996]. For patients treated with Metformin, surgical procedures may contribute to the development of lactic acidosis [Mears et al. 2002; Mercker et al. 1997], with hypotension secondary to blood loss or anaesthetic agents, associated myocardial ischaemia and sepsis being contributory factors [Chan and Feher 1999]. Cessation of Metformin prior to major surgery is common practice, but there is no evidence for the benefit of this nor consensus on the duration of Metformin withdrawal. Given that prolonged omission of Metformin will result in deterioration of glycaemic control, it seems reasonable to recommend ceasing Metformin on the day of major surgery, and resuming this 24 hours post-operatively, providing that the serum creatinine level has not risen significantly. Glycaemic control can be maintained with an I-G infusion until Metformin is resumed or alternative therapy commenced.

On the other hand, there is no evidence that the continuation of Metformin during the peri-operative period is hazardous for patients who are undergoing minor surgery although caution may be required for patients with significant cardiac or hepatic disease or minor renal impairment,. Ultimately, clinicians should use their discretion in deciding whether Metformin should be withdrawn for individual patients, but alternative arrangements for maintaining glycaemic control will need to be made.

Metformin and Intravenous Radio-Contrast

- Contrast-induced nephropathy may result in lactic acidosis especially in patients taking metformin.
- Serum creatinine should be checked before metformin is restarted following intravenous radio-contrast administration.

- The risk of lactic acidosis following intravenous contrast administration for patients with normal renal function is low.

Patients with diabetes are prone to contrast-induced nephropathy. Radiological procedures involving the intravascular administration of contrast media, may precipitate renal failure with subsequent lactic acidosis in patients taking Metformin [Jamet et al. 1980; Klow et al. 2001; McCartney et al. 1999]. Most radiological services recommend routine omission of Metformin for 24 hours prior to the procedure and the withholding of Metformin for 48 hours afterwards. Prolonged cessation of Metformin may result in hyperglycaemia which may result in dehydration, thereby increasing the risk of contrast-medicated nephropathy. Metformin associated lactic acidosis following intravenous contrast media, occurs almost exclusively in patients who have pre-existing renal impairment [Thomsen and Morcos 1999] and it is therefore essential that the serum creatinine level is known prior to the radiological procedure. For patients whose serum creatinine levels are known to be less than 130μmol/l prior to the radiological procedure, provided facilities are available to monitor the patients' creatinine level afterwards, it may be reasonable to continue Metformin [McCartney et al. 1999]. This should be discussed with the radiologist. However, given the lack of evidence concerning the efficacy and duration of metformin withdrawal, it seems reasonable to withhold metformin in those with mild renal impairment (serum creatinine 110-160 μmol/L) for 48 hours following the procedure (and not prior) and to resume metformin once it is known that renal function has not deteriorated. Following the procedure, the clinician who requested the procedure should ensure that the serum creatinine level has not increased significantly before Metformin is resumed. For patients with mild renal impairment receiving metformin, it may be appropriate to review the continued use of metformin anyway, and change to alternative anti-hyperglycaemic therapy.

BOWEL PREPARATION

- The dose of insulin should be reduced during the period of bowel preparation.
- Short-acting insulin and oral AHG medication should be withheld.
- Clear fluids should contain glucose, and diet drinks are consumed if the BGL is elevated.
- Patients with unstable diabetes should be admitted to hospital during the period of bowel preparation and an I-G infusion commenced.

Patients undergoing colonoscopy or bowel surgery are usually required to consume clear fluids for at least one day before their procedures. To avoid hypoglycaemia, oral AHG therapy should be withheld during the period of clear fluid ingestion. Patients receiving insulin therapy generally require a smaller dose of insulin, given their reduced carbohydrate intake (Table 1). In summary:

1. Those patients receiving short-acting insulin before each meal with intermediate-acting insulin at night should replace the short-acting insulin with an injection of intermediate-acting insulin in the morning (half the sum of the three short-acting insulin doses), while

the night-time intermediate-acting insulin dose may remain the same. Alternatively, the doses of quick-acting insulin could be reduced by 50% and the intermediate or long-acting insulin dose reduced by 1/3rd.

2. Patients receiving a combination of short and intermediate acting insulin in the morning and evening should omit their short-acting insulin and continue with the same dose of intermediate acting insulin. An alternate approach might be to reduce both doses by 50%, analogous to the recommendations for patients receiving pre-mixed insulins.

3. Patients who take Glargine (either in the morning or in the evening) in combination with short-acting insulin should continue to take Glargine but the short-acting insulin should be omitted.

4. For those on pre-mixed insulin, half the morning and evening doses of insulin should be given.

More frequent BGL monitoring is essential, and patients who normally have unstable glycaemic control should perform second hourly BGL testing. If BGLs become erratic, patients must have access to medical advice. "Clear fluids" should contain some glucose and not purely "diet drinks" or "diet jelly". Drinks containing added glucose should be consumed if the BGL falls below 5.0mmol/l. On the other hand, fluids containing less glucose (eg broths or diet drinks) should be consumed if the BGL exceeds 10mmol/L. A summary of recommendations for patients with diabetes during bowel preparation is shown in table 2.

For patients receiving a large dose of insulin or who have poorly controlled diabetes, it may be more appropriate to admit them to hospital during the clear fluids stage and commence an I-G infusion.

THE POST-OPERATIVE PERIOD

- Insulin-glucose infusions should be continued until the patients can resume an adequate diet.

- I-G infusions should ideally be stopped after breakfast, and a dose of subcutaneous insulin (or oral AHG) is given before breakfast.

- Hyperglycaemia detected post-operatively in patients not previously known to have diabetes should be managed as if diabetes was present, and the diagnosis of diabetes reconsidered once the patient has recovered from their surgery.

- Diabetes medication requirements may be increased (or occasionally decreased) in the post-operative period, and frequent BGL monitoring is therefore essential.

- Diabetes management expertise must be available for the post-operative management of glycaemic instability.

After the surgical procedure, the insulin-glucose infusion should be continued until the patient can tolerate an adequate oral intake (at last 50% of their usual diet). The I-G infusion should be continued whilst the patient is only able to tolerate clear fluids. When solid food is commenced, give the patient's usual dose of subcutaneous insulin prior to the meal and the I-G infusion can then be ceased 1-2 hours afterwards (allowing for some overlap between intravenous and the absorption of the subcutaneous insulin). It is preferable to resume subcutaneous insulin and cease the infusion with breakfast, especially when pre-mixed or intermediate-acting insulin is usually given in the morning, and given the greater availability of medical and nursing staff during daytime hours should glycaemic control become unstable. If a patient normally injects their Lantus insulin at night, yet resumes s.c. insulin and eating in the morning, then a reduced dose (say 1/3rd of the usual evening dose) of Lantus could be given that morning, with the usual dose of Lantus given that night. Oral AHG therapy can also be restarted when patients resume eating.

Facilities should exist for the overnight admission of insulin–treated patients (especially those with type 1 diabetes) that have undergone day-only procedures if the resumption of oral intake is delayed or if glycaemic control becomes unstable.

During the post-operative period, insulin requirements may fluctuate, depending on the metabolic impact of the procedure, the presence of pain or infection and the adequacy of oral intake. Whilst this is difficult to anticipate in all patients, the best approach following major surgery is to resume the patient's usual diabetes medication after ceasing the I-G infusion, and to provide additional treatment (insulin) should glycaemic thresholds be exceeded. It is essential that BGLs be monitored more frequently during this period and treatment requirements be reviewed on a daily basis. Should oral intake not be adequate and hypoglycaemia occur, the next dose of insulin should **not** be omitted (otherwise hyperglycaemia and possible ketosis may occur). Rather, the dose of insulin could be reduced by ~10% and the whole insulin treatment regimen reviewed. When oral intake is variable or unreliable, a basal-bolus insulin regimen is more appropriate, as the basal insulin can be continued, and the timing and doses of quick-acting insulin adapted according to the patients carbohydrate intake.

Many patients with diabetes not previously treated with insulin who require insulin in the post-operative period will also require insulin after discharge from hospital. Thus it is important to commence self-injection education for the patient as early as possible, in order to avoid delaying the patient's discharge unnecessarily.

Patients with diabetes that was poorly controlled (HbA1c ≥8%) prior to admission should have their treatment reviewed and adjusted as appropriate either during their admission (major surgery) or following discharge (minor surgery).

Patients not previously known to have diabetes who are found to be hyperglycaemic post-operatively, should have their HbA1c measured and be managed as if they had diabetes until they have recovered from their surgery and resumed their usual diet and activity. If their HbA1c is ≥7%, then it is likely that diabetes was present, but undiagnosed, prior to admission. It should not be assumed that post-operative hyperglycaemia in someone not previously known to have diabetes is a stress response that does not require treatment and that does not require further evaluation after discharge from hospital.

Following discharge from hospital, patients must be able to obtain expert advice should their glycaemic control become unstable and early follow-up after discharge from hospital should be organised.

The post-operative care of insulin-treated patients following Caesarian Section should be considered as part of the management of "diabetes during pregnancy". This requires a different approach and hence will not be discussed in this document.

"Sliding Scale Insulin"

- "Sliding scale insulin" is **NOT** recommended for the post-operative management of diabetes when used as sole therapy
- A "supplemental insulin protocol", which is given in addition to the patient's usual diabetes medication regimen, is more appropriate.

In many institutions, a "sliding scale insulin" regimen has traditionally been used to manage hyperglycaemia, often in the post-operative setting. This involves the administration of prescribed doses of insulin when the BGL is within specified ranges, with insulin often being withheld when the BGL is within the normal range. The main problem with this approach is that, when given as sole therapy, it is retrospective and aimed at correcting rather than preventing hyperglycaemia. It usually results in under-insulinisation (and therefore hyperglycaemia), especially if opportunities to administer insulin are missed or insulin is not given when the blood glucose level is 'normal' (or low). In addition, the frequency of insulin administration is often not specified. Attention is not paid to the timing of insulin in relation to meals, nor is there any consideration of the pharmacokinetics of the injected insulin or of the individual patient's insulin sensitivity. The frequency of insulin administration is also dependent on the timing of BGL monitoring by the nursing staff. The "sliding scale insulin" approach is often a "set and forget" process and is usually not reviewed or adjusted by the medical team. "Sliding scale insulin", when used as sole therapy, can lead to inadequate, inappropriate or indiscriminate insulin administration, resulting in large swings in blood glucose levels without contributing to any understanding of the patient's true daily insulin requirement [Queale et al. 1997]. "Sliding scale insulin" is not recommended for the management of post-operative hyperglycaemia.

On the other hand, given the changing insulin requirements in the post-operative setting, there may be a place for a "supplemental insulin regimen". This is based on the patient's usual (or recently prescribed) insulin / oral AHG regimen, with provisions for supplemental or additional insulin if the BGL exceeds a certain threshold. This supplemental insulin is always in the short- or rapid-acting form and given before meals and supper. It is additional to any insulin already prescribed at that time, and it is reliant on BGL monitoring being performed at pre-determined time points. It is essential that daily medical review of the patient's BGLs and insulin requirements is undertaken, thereby enabling appropriate adjustment of the patient's insulin doses for the subsequent day.

In a recent study of non-surgical patients with Type 2 Diabetes, a basal bolus regimen using Glargine as the basal insulin and a rapid-acting analogue (Glulisine) with meals, with provision for supplemental rapid-acting insulin, was shown to be superior to a traditional sliding scale regimen using regular insulin 4 times per day in achieving and maintaining glycaemic control. [Umpierrez et al, 2007]. This study utilized 0.2-0.25 units/Kg body weight/day as basal insulin (Glargine) and 0.2-0.25 units/Kg body weight/day as prandial insulin (Glulisine) with one third of this given before each meal. Supplemental Glulisine was given with each meal and supper if required. Whilst this study did not specifically address post-operative blood glucose control, it would be reasonable to use such an insulin regimen in the initial management of post-operative hyperglycaemia, following cessation of the I-G infusion, in the previously insulin-naive patient whose insulin requirements are unknown. Such patients might include those not previously known to have diabetes, those with poor glycaemic control prior to admission, and those patients previously treated with more than one type of oral AHG who have undergone major surgery. For patients whose oral intake may not yet have returned to normal, this approach also has the benefit of providing some flexibility with the dose and timing of the rapid-acting analogue insulin according to the quantity and timing of carbohydrate ingestion, whilst providing a constant dose of basal long-acting analogue insulin. The key feature of this approach is the use of basal insulin. Once blood glucose control has been established, this regimen can be modified if necessary prior to discharge.

RADIOLOGICAL PROCEDURES

- Patients with diabetes should undergo those radiological procedures that involve a period of fasting early in the morning
- For procedures performed later in the day, fasting for patients with diabetes should not be for greater than 4 hours, and diabetes medications should be reduced during the period of fasting.
- Special guidelines should be developed for patients undergoing stress sestamibi and positron emission tomography scans.

For procedures such as CT scan or ultrasound of abdomen, patients are usually told to fast for 4 hours prior to the procedure. In order to minimize the disruption to their glycaemic control, patients with diabetes should undergo such radiological procedures early in the morning, and their diabetes medication(s) and breakfast should be delayed until after the procedure is completed (see table 2). Diabetes medications (both insulin and oral AHG agents) can be resumed with the next meal (usually a 'late breakfast' by 1000 hrs). The issues regarding metformin have been discussed previously in Section H3.

If this is not possible and the procedure is performed later in the day, patients should commence fasting after breakfast and their diabetes medication in the morning should be reduced. Oral AHG therapy should be withheld in the morning. Insulin-treated patients should be managed as for minor surgery in the afternoon and the morning dose of insulin should be reduced by 50%. If the

study is held in the early afternoon, the patients should have a mid-morning snack 4 hours prior to the scheduled procedure.

For patients undergoing a sestamibi scan for evaluation of myocardial ischaemia, the rest and stress studies should be done on separate days to reduce the duration of fasting. For insulin-treated patients, half the usual morning dose of insulin can be given followed by an early breakfast. This is similar to the protocol for patients who have surgical procedures in the afternoon. Patients usually need to fast for at least 4 hours, but the procedure should finish before lunch. Blood glucose should be monitored every 2 hours whilst patients are fasting and undergoing the scan. For patients whose diabetes control is brittle, the stress sestimibi study should be performed in a Nuclear Medicine Unit within a hospital where an I-G infusion can be commenced should the patients' glycemic control become unstable.

Positron Emission Tomography (PET) scans using the radio-isotope fluorine-18-fluorodeoxyglucose (FDG) can be difficult for patients with diabetes, as acute hyperglycaemia and insulin therapy at the time of the study can interfere with the uptake of FDG to the area of interest [Lindholm et al. 1993; Ishizu et al. 1994; Zhuang et al. 2001]. It is therefore especially important to ensure these patients have stable glycaemic control prior to their PET study.

For hospital inpatients, both patients and staff are often not informed in advance of the exact time of radiological procedures and it is therefore difficult to plan appropriate adjustments to their diabetes medications. Procedures are often delayed or performed at short notice, such that it is not possible to delay or reduce insulin doses. To avoid hypoglycaemia, patients may require an intravenous glucose infusion when fasting commences until they resume their regular oral intake after the procedure. Subsequent insulin doses may also need to be modified until oral intake is resumed. If the fast is prolonged more than 1 hour past the time when the next injection of insulin is due to be given, then an insulin-glucose infusion should be commenced. All inpatients treated with insulin or oral AHG agents, but particularly those who are insulin-treated, should have their BGLs monitored every hour while fasting in this setting. Good communication between the radiology department and medical and nursing staff is essential in order to avoid major disruptions to glycaemic control in such situations.

CONCLUSION

In conclusion, maintaining good glycaemic control during the peri-operative period results in improved outcomes following surgery. In order to keep blood glucose levels within the target range, diabetes medications often need to be altered immediately before and following surgical and radiological procedures. There may be great individual variation in the impact of surgery and the adjustments to therapy required, depending on the pre-existing diabetes status of the patient, the nature of the surgery and the presence of post-operative complications. Therefore, management of patients with diabetes in the peri-operative period is complex, and requires a close working relationship and effective communication between surgeons, physicians and anaesthetists. As the incidence of diabetes in Australia rises, this will become an increasingly important challenge faced by clinicians.

REFERENCES

Axelrod, D. A., Upchurch, G. R., Jr., DeMonner, S., Stanley, J. C., Khuri, S., Daley, J., Henderson, W. G., and Hayward, R. (2002). "Perioperative cardiovascular risk stratification of patients with diabetes who undergo elective major vascular surgery." *J Vasc Surg*, 35(5), 894-901.

Babineau, T. J., and Bothe, A., Jr. (1995). "General surgery considerations in the diabetic patient." *Infect Dis Clin North Am*, 9(1), 183-93.

Bailey, C. J., and Turner, R. C. (1996). "Metformin." *N Engl J Med*, 334(9), 574-9.

Capes, S. E., Hunt, D., Malmberg, K., and Gerstein, H. C. (2000). "Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview." *Lancet*, 355(9206), 773-8.

Capes, S. E., Hunt, D., Malmberg, K., Pathak, P., and Gerstein, H. C. (2001). "Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview." *Stroke*, 32(10), 2426-32.

Chan, N. N., and Feher, M. D. (1999). "Metformin and perioperative risk." *Br J Anaesth*, 83(3), 540-1.

Dronge, A. S., Perkal, M. F., Kancir, S. Concato, J., Aslan, M., Rosenthal, R. A. (2006) "Long-term glycemic control and postoperative infectious complications." *Arch Surg* 141, 375-380.

Furnary, A. P., Gao, G., Grunkemeier, G. L., Wu, Y., Zerr, K. J., Bookin, S. O., Floten, H. S., and Starr, A. (2003). "Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting." *J Thorac Cardiovasc Surg*, 125(5), 1007-21.

Golden, S. H., Peart-Vigilance, C., Kao, W. H., and Brancati, F. L. (1999). "Perioperative glycemic control and the risk of infectious complications in a cohort of adults with diabetes." *Diabetes Care*, 22(9), 1408-14.

Guvener, M., Pasaoglu, I., Demircin, M., and Oc, M. (2002). "Perioperative hyperglycemia is a strong correlate of postoperative infection in type II diabetic patients after coronary artery bypass grafting." *Endocr J*, 49(5), 531-7.

Ishizu, K., Nishizawa, S., Yonekura, Y., Sadato, N., Magata, Y., Tamaki, N., Tsuchida, T., Okazawa, H., Miyatake, S., and Ishikawa, M. (1994). "Effects of hyperglycemia on FDG uptake in human brain and glioma." *Journal of Nuclear Medicine*, 35(7), 1104-9.

Jamet, P., Lebas de Lacour, J. C., Christoforov, B., and Stern, M. (1980). "Fatal case of metformin-induced lactic acidosis after urography in a diabetic patient." *Sem Hop*, 56(9-10), 473-4.

Janand-Delenne, B., Savin, B., Habib, G., Bory, M., Vague, P., and Lassmann-Vague, V. (1999). "Silent myocardial ischemia in patients with diabetes: who to screen." *Diabetes Care*, 22(9), 1396-400.

Juul, A. B., Wetterslev, J., Kofoed-Enevoldsen, A., Callesen, T., Jensen, G., and Gluud, C. (2004b). "The Diabetic Postoperative Mortality and Morbidity (DIPOM) trial: rationale and design of a multicenter, randomized, placebo-controlled, clinical trial of metoprolol for patients with diabetes mellitus who are undergoing major noncardiac surgery." *Am Heart J*, 147(4), 677-83.

Klow, N. E., Draganov, B., and Os, I. (2001). "[Metformin and contrast media--increased risk of lactic acidosis?]." *Tidsskr Nor Laegeforen*, 121(15), 1829.

Lazar, H. L., Chipkin, S. R., Fitzgerald, C. A., Bao, Y., Cabral, H., and Apstein, C. S. (2004). "Tight glycemic control in diabetic coronary artery bypass graft patients improves perioperative outcomes and decreases recurrent ischemic events." *Circulation*, 109(12), 1497-502.

Lindholm, P., Minn, H., Leskinen-Kallio, S., Bergman, J., Ruotsalainen, U., and Joensuu, H. (1993). "Influence of the blood glucose concentration on FDG uptake in cancer - a PET study." *Journal of Nuclear Medicine*, 34(1), 6-11.

Ljungqvist, O., Nygren, J., Soop, M., and Thorell, A. (2005). "Metabolic perioperative management: novel concepts." *Current Opinion in Critical Care*, 11(4), 295-299.

Marks, J. B. (2003). "Perioperative management of diabetes." *Am Fam Physician*, 67(1), 93-100.

McAlister, F. A., Man, J., Bistritz, L., Amad, H., and Tandon, P. (2003). "Diabetes and coronary artery bypass surgery: an examination of perioperative glycemic control and outcomes." *Diabetes Care*, 26(5), 1518-24.

McCartney, M. M., Gilbert, F. J., Murchison, L. E., Pearson, D., McHardy, K., and Murray, A. D. (1999). "Metformin and contrast media--a dangerous combination?" *Clin Radiol*, 54(1), 29-33.

Mears, S. C., Lipsett, P. A., Brager, M. D., and Riley, L. H., 3rd. (2002). "Metformin-associated lactic acidosis after elective cervical spine fusion: a case report." *Spine*, 27(22), E482-4.

Mercker, S. K., Maier, C., Neumann, G., and Wulf, H. (1997). "Lactic acidosis as a serious perioperative complication of antidiabetic biguanide medication with metformin." *Anesthesiology*, 87(4), 1003-5.

Nathan, D.M., Kuenen, J., Borg, R. Zheng, H. Schoenfeld, D. Heine, R.J. (2008) "Translating the A1c assay into estimated average glucose values" *Diabetes Care*, 31, 1473-1478

NICE-SUGAR Study Investigators, Finfer, S., Chittock, D. R., Su, S.Y., Blair, D., Foster, D., Dhingra, V., Bellomo, R., Cook, D., Dodek, P., Henderson, W. R., Hébert , P. C., Heritier, S., Heyland, D. K., McArthur, C., McDonald, E., Mitchell, I., Myburgh, J. A., Norton, R., Potter, J., Robinson, B. G., Ronco, J. J.. (2009). "Intensive versus conventilnal glucose control in critically ill patients." *New Engl J Med*, 360(13), 1283-97

Pomposelli, J. J., Baxter, J. K., 3rd, Babineau, T. J., Pomfret, E. A., Driscoll, D. F., Forse, R. A., and Bistrian, B. R. (1998). "Early postoperative glucose control predicts nosocomial infection rate in diabetic patients." *J Parenter Enteral Nutr*, 22(2), 77-81.

Queale, W. S., Seidler, A. J., and Brancati, F. L. (1997). "Glycemic control and sliding scale insulin use in medical inpatients with diabetes mellitus." *Arch Intern Med*, 157(5), 545-52.

Sandler, R. S., Maule, W. F., and Baltus, M. E. (1986). "Factors associated with postoperative complications in diabetics after biliary tract surgery." *Gastroenterology*, 91(1), 157-62.

The ACE/ADA Task Force on Inpatient Diabetes (2006) "American College of Endocrinology and American Diabetes Association consensus statement on inpatient diabetes and glycemic control: a call to action" *Diabetes Care*, 29(8), 1955-1962.

Thomsen, H. S., and Morcos, S. K. (1999). "Contrast media and metformin: guidelines to diminish the risk of lactic acidosis in non-insulin-dependent diabetics after administration of contrast media. ESUR Contrast Media Safety Committee." *Eur Radiol*, 9(4), 738-40.

Tokumine, J., Sugahara, K., Fuchigami, T., Teruya, K., Nitta, K., Satou, K. (2005) "Unanticipated full stomach at anesthesia induction in a type I diabetic patient with asymptomatic gastroparesis." *J Anesth* 19(3), 247-8.

Umpierrez, G. E., Isaacs, S. D., Bazargan, N., You, X., Thaler, L. M., and Kitabchi, A. E. (2002). "Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes." *J Clin Endocrinol Metab*, 87(3), 978-82.

Umpierrez, G. E., Smiley, D., Zisman, A., Prieto, L. M., Palacio, A., Ceron, M., Puig, A., Mejia, R. (2007). "Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes (RABBIT 2 trial)" *Diabetes Care* 30(9), 2181-6.

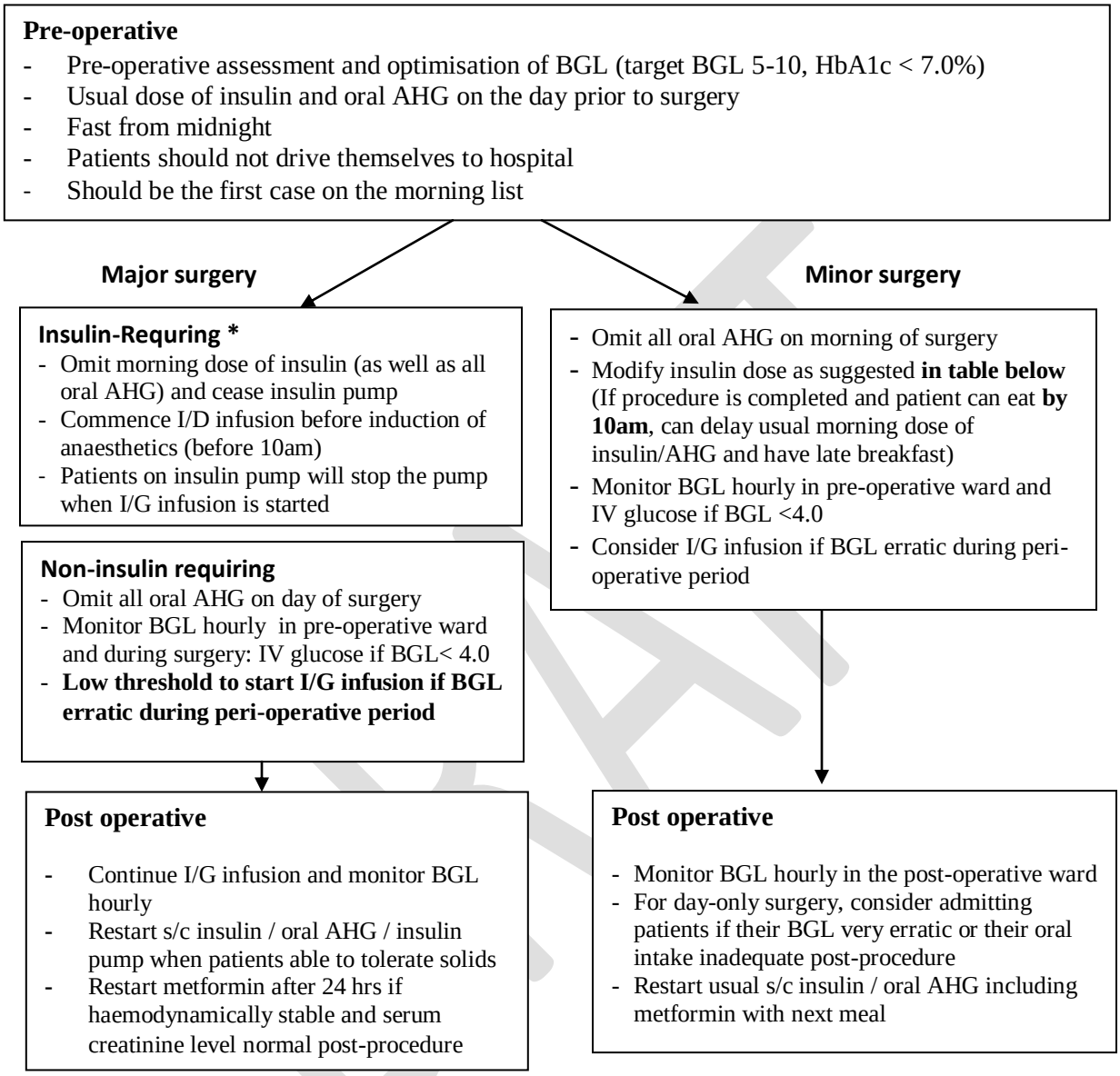
van den Berghe, G., Wouters, P., Weekers, F., Verwaest, C., Bruyninckx, F., Schetz, M., Vlasselaers, D., Ferdinande, P., Lauwers, P., and Bouillon, R. (2001). "Intensive insulin therapy in the critically ill patients." *N Engl J Med*, 345(19), 1359-67.

Virkkunen, J., Heikkinen, M., Lepantalo, M., Metsanoja, R., and Salenius, J. P. (2004). "Diabetes as an independent risk factor for early postoperative complications in critical limb ischemia." *J Vasc Surg*, 40(4), 761-7.

Zerr, K. J., Furnary, A. P., Grunkemeier, G. L., Bookin, S., Kanhere, V., and Starr, A. (1997). "Glucose control lowers the risk of wound infection in diabetics after open heart operations." *Ann Thorac Surg*, 63(2), 356-61.

Zhuang, H. M., Cortes-Blanco, A., Pourdehnad, M., Adam, L. E., Yamamoto, A. J., Martinez-Lazaro, R., Lee, J. H., Loman, J. C., Rossman, M. D., and Alavi, A. (2001). "Do high glucose levels have differential effect on FDG uptake in inflammatory and malignant disorders?" *Nucl Med Commun*, 22(10), 1123-8.

Figure 1: Summary of Peri-Operative Protocol for Patients on the Morning list

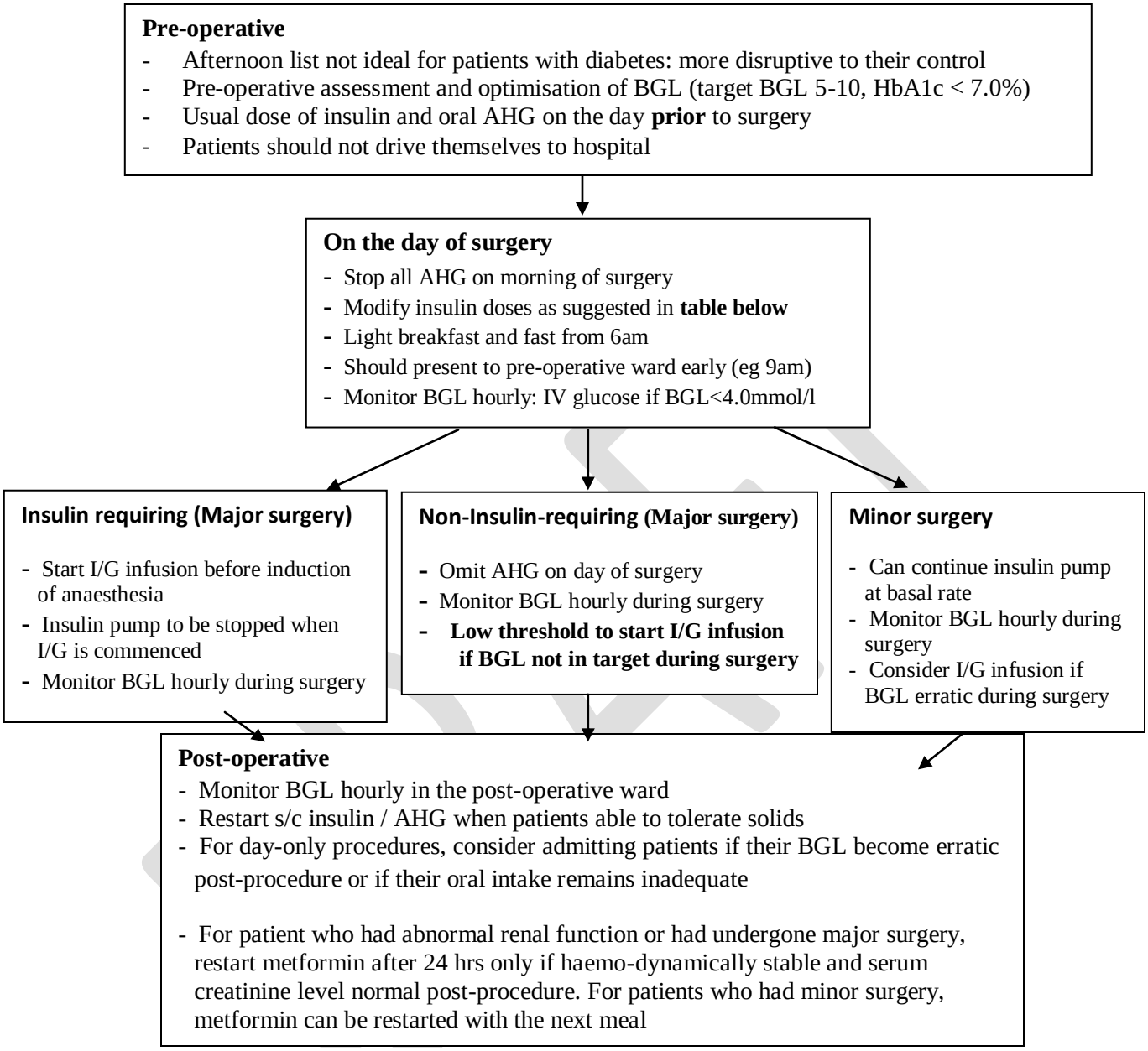


Insulin regimen	Suggested modification for minor surgery
AHG and night time Glargine/ Detemir/ Isophane only	Stop AHG and give usual dose of insulin night before. May reduce dose by 10% if recent fasting BGL consistently <5.0mmol/l
Meal-time bolus insulin and night-time Isophane / Detemir	½ combined morning and lunch time bolus insulin dose but given as intermediate-acting insulin in the morning
Meal-time bolus and morning Glargine / Detemir/ Isophane	Omit bolus insulin in the morning and give usual morning dose of intermediate- or long-acting insulin

* Includes patients with type 1 diabetes as well as insulin-requiring type 2 diabetes

Abbreviations:
I/G: Insulin-glucose infusion. **AHG**: Anti-hyperglycaemic agents **BGL**: Blood glucose level

Figure 2: Summary of Peri-Operative Protocol for Patients on the Afternoon List



Insulin regimen	**Suggested modification**
AHG and night time Glargine/ Detemir/ Isophane only	Stop AHG and give usual dose of insulin night before. May reduce dose by 10% if recent fasting BGL consistently <5.0mmol/l
Meal-time bolus insulin and night-time Isophane / Detemir	½ morning bolus insulin dose; as well as ½ lunch time bolus insulin dose but given as Isophane/ Detemir before light breakfast
Meal-time bolus insulin and morning Glargine / Detemir/ Isophane	½ morning bolus insulin dose; and give ½ morning intermediate- or long-acting insulin dose before light breakfast
Meal-time bolus and night-time Glargine	½ morning bolus insulin dose before light breakfast; and give usual dose of Glargine the night before
Pre-mixed Insulin	½ usual morning dose of insulin

Table 1: Bowel preparation for patients with diabetes: while patients are on clear fluids

- Omit all AHG
- If patients are on insulin, modify insulin regimen as below:

Insulin Regimen	
Short-acting insulin (with meals) and Glargine	Omit short acting insulin and continue Glargine
Short-acting insulin (with meals) and Detemir/ Isophane twice daily	Omit short-acting insulin and continue Detemir /Isophane twice daily
Short-acting insulin (with meals) and Detemir/ Isophane at night only	½ sum of all meal time short-acting insulin and administer as Detemir/ Isophane in the morning Continue Detemir/ Isophane in the evening/night
Pre-mixed insulin	½ the Pre-mixed insulin doses
Insulin pump	Continue at the basal infusion rate

- More frequent BGL monitoring (every 2 hours)
- May consume glucose-containing fluid or jelly
- Add extra glucose in fluid if BGL < 5.0mmol/l
- Avoid diet drinks or diet jelly unless BGL > 10mmol/l
- Consider admitting patients with unstable glycaemic control to hospital during the period of clear fluid
- Patients must have access to their diabetes physician or diabetes center for advice

Table 2: Summary of protocol for patients with diabetes undergoing radiological studies

<table>
<tr><td>Morning study</td><td colspan="2">- Ensure staff at radiology facility aware of the patients' diabetes status
- Usual diabetes medications the day before, and fast from midnight
- Schedule radiological study for the first appointment in the morning (should complete study prior to 10am)
- Once radiological study is completed, patients can administer usual morning diabetes medications (AHG or insulin) and have breakfast
- Special issues with metformin *</td></tr>
<tr><td rowspan="4">Study mid morning or early afternoon</td><td colspan="2">- Not ideal and need to negotiate with radiologist
- Ensure staff at radiology facility aware of the patients' diabetes status
- Can have breakfast and commence fasting (for 4 hours before study)</td></tr>
<tr><td>Insulin requiring</td><td>- half the usual morning dose of insulin (protocol as per that for insulin-requiring patients in table 2)</td></tr>
<tr><td>Oral AHG</td><td>- omit morning dose of AHG
- Special issues with metformin*</td></tr>
<tr><td colspan="2">- Patient should not drive to the radiology facility while fasting
- More frequent BGL monitoring during fasting and at the radiology facility: aim to keep BGL 5 – 10mmol/l</td></tr>
<tr><td rowspan="4">Stress sestamibi scan</td><td colspan="2">- Should have stress and rest studies on separate days to minimize duration of fasting
- Ensure staff at radiology facility aware of the patients' diabetes status
- Can have early breakfast and fast for 4 hours thereafter</td></tr>
<tr><td>Insulin requiring</td><td>- Half the usual morning dose of insulin (protocol as per that in insulin-requiring patients in Figure 1)</td></tr>
<tr><td>Oral AHG</td><td>- Omit morning dose of AHG
- Metformin can be restarted after the study</td></tr>
<tr><td colspan="2">- Patient should not drive to the radiology facility while fasting
- More frequent BGL monitoring during fasting and at the radiology facility: aim to keep BGL 5 – 10mmol/l
- Consider performing the study in a Nuclear Medicine Unit of a hospital for those with unstable diabetes (ie, allows commencement of insulin-dextrose infusion if BGL becomes erratic)</td></tr>
</table>

* If study involves intravenous contrast, the requesting clinician should provide the most recent serum creatinine level to the radiologist. Metformin may be omitted on day of study, and ensure serum creatinine level assessed post-procedure before restarting metformin

Examples of insulin adjustment

Minor Surgery (eg, cystoscopy), Morning List:

Usual Insulin Regimen:

Aspart insulin 10 units before breakfast

Aspart insulin 10 units before lunch

Aspart insulin 12 units before dinner

Isophane insulin 40 units before bed

Fast from 12 midnight the day before surgery

On the day of surgery:

Morning insulin = ½ x (10 + 10) units = **10 units isophane**

Following procedure, if patient ready to have lunch, give half the usual lunch-time dose: ½ x 10 units = **5 units Aspart insulin**

Continue usual dose of insulin before dinner and before bed

Minor Surgery (eg, total hip replacement), Afternoon List

Usual Insulin Regimen:

Mixtard 30/70 - 30 units before breakfast

Mixtard 30/70 - 16 units before dinner

Metformin 100mg twice a day

On day of surgery:

Morning insulin: ½ X 30 units = **15 units Mixtard 30/70** before light breakfast (prior to 6am)

Omit Metformin in the morning

Fast from 6am

Present to Pre-operative ward by 9am

Monitor BGL 2 hourly by staff

Can have usual dose of Mixtard 30/70 and Metformin in the evening

Major Surgery (eg, total thyroidectomy), Afternoon List:

Usual Insulin Regimen:

Insulin Lispro 16 units before breakfast

Insulin Lispro 12 units before lunch

Insulin Lispro 12 units before dinner

Glargine 20 units before bed

On the day of surgery:

Usual dose of Glargine the night before

Morning insulin = ½ x 16 units = **8 units Insulin Lispro**

before light breakfast (prior to 6am)

Fast from 6am

Present to Pre-operative ward by 9am

Monitor BGL 2 hourly by staff

Commence insulin-dextrose infusion prior to induction of anaesthetics