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Position Statement/Recommendations

# Practical management of diabetes patients before, during and after surgery: A joint French diabetology and anaesthesiology position statement

E. Cosson [a,b], B. Catargi [c,*], G. Cheisson [d], S. Jacqueminet [e,f], C. Ichai [g,h], A.-M. Leguerrier [i], A. Ouattara [j,k], I. Tauveron [l,m,n,o], E. Bismuth [p], D. Benhamou [d], P. Valensi [a]

[a] *Département d'endocrinologie-diabétologie-nutrition, CRNH-IdF, CINFO, hôpital Jean-Verdier, université Paris 13, Sorbonne Paris Cité, AP–HP, 93140 Bondy, France*
[b] *UMR U1153 Inserm, U1125 Inra, CNAM, université Paris 13, Sorbonne Paris Cité, 93000 Bobigny, France*
[c] *Service d'endocrinologie-maladies métaboliques, hôpital Saint-André, CHU de Bordeaux, 1, rue Jean-Burguet, 33000 Bordeaux, France*
[d] *Service d'anesthésie-réanimation chirurgicale, hôpitaux universitaires Paris-Sud, hôpital de Bicêtre, AP–HP, 78, rue du Général-Leclerc, 94275 Le Kremlin-Bicêtre, France*
[e] *Institut de cardio-métabolisme et nutrition, hôpital de la Pitié-Salpêtrière, AP–HP, 75013 Paris, France*
[f] *Département du diabète et des maladies métaboliques, hôpital de la Pitié-Salpêtrière, 75013 Paris, France*
[g] *Service de la réanimation polyvalente, hôpital Pasteur 2, CHU de Nice, 30, voie Romaine, 06001 Nice cedex 1, France*
[h] *IRCAN, Inserm U1081, CNRS UMR 7284, university hospital of Nice, 06000 Nice, France*
[i] *Service de diabétologie-endocrinologie, CHU hôpital Sud, CHU de Rennes, 16, boulevard de Bulgarie, 35056 Rennes, France*
[j] *Department of anaesthesia and critical care II, Magellan medico-surgical center, CHU de Bordeaux, 33000 Bordeaux, France*
[k] *Inserm, UMR 1034, biology of cardiovascular diseases, université Bordeaux, 33600 Pessac, France*
[l] *Service d'endocrinologie-diabétologie, CHU de Clermont-Ferrand, 58, rue Montalembert, 63000 Clermont-Ferrand, France*
[m] *UFR médecine, université Clermont-Auvergne, 28, place Henri-Dunant, 63000 Clermont-Ferrand, France*
[n] *UMR CNRS 6293, Inserm U1103, génétique reproduction et développement, université Clermont-Auvergne, 63170 Aubière, France*
[o] *Endocrinologie-diabétologie, CHU G.-Montpied, BP 69, 63003 Clermont-Ferrand, France*
[p] *Service d'endocrinologie-pédiatrie-diabète, hôpital Robert-Debré, AP–HP, 75019 Paris, France*

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## Abbreviations

| | |
|---|---|
| ACR | albumin-to-creatinine ratio |
| CAN | cardiac autonomic neuropathy |
| BNP | brain natriuretic peptide |
| CSII | continuous subcutaneous insulin infusion |
| GDM | gestational diabetes mellitus |
| GLP-1 | glucagon-like peptide 1 |
| GP | general practitioner |
| HF | heart failure |
| ICU | intensive care unit |
| ISPAD | International Society for Pediatric and Adolescent Diabetes |
| IU | international unit(s) |
| IV | intravenous |
| IVII | intravenous insulin infusion |
| SFAR | French Society of Anaesthesia and Resuscitation |
| OAD | oral antidiabetic drug |
| PACU | post-anaesthesia care unit |
| SC | subcutaneous |
| SFAR | French Society of Anaesthesia and Intensive Care |
| SFD | French-Speaking Society of Diabetes |
| SMI | silent myocardial ischaemia |
| T1D | type 1 diabetes |
| T2D | type 2 diabetes |

* Corresponding author. Unité cardiovasculaire et d'endocrino-diabétologie, hôpital Saint-André, CHU de Bordeaux, 1, rue Jean-Burguet, 33000 Bordeaux, France.
*E-mail address:* bogdan.catargi@chu-bordeaux.fr (B. Catargi).

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## Introduction

Diabetes is a worldwide disorder. Despite huge advances in care management, diabetes patients may nevertheless suffer from cardiovascular and microvascular complications, which may explain their need for surgery more often than non-diabetes patients. Likewise, known or unknown diabetes increases perioperative risks from, for example, the surgical procedures themselves, anaesthetic drugs, fasting, infusions, associated treatment and stress.

Therefore, diabetes patients should be given special attention before, during and after surgery. In this context, experts from both the French-Speaking Society of Diabetes (SFD; Société francophone du diabète) and French Society of Anaesthesia and Resuscitation (SFAR; Société française d'anesthésie et de réanimation) met to devise the following guidelines. The full text is published in French and English, with 20 pages created by the Working Group to illustrate how the guidelines apply in daily practice (http://sfar.org/gestion-du-patient-diabetique/). The present report is a comprehensive support text particularly dedicated to diabetologists not only for their own uses, but also as an educational tool to communicate with anaesthesiologists.

## Materials and methods

A group of experts (six diabetologists: E.C., B.C., S.J., A.M.L., I.T., P.V.; and four anaesthesiologists: D.B., C.G., C.I., A.O.) met twice a year between November 2014 and April 2017 in Paris, France, to review the literature, and discuss and write the text of the following expert opinion. Due to the limited number of validated studies, recommendations were not graded and the text should be considered expert advice.

## Results

### *Preoperative management of adult patients with diabetes*

#### *Identification of patients with diabetes and at risk for stress hyperglycaemia*

*Known diabetes: different types, main acute complications and treatment (what should anaesthesiologists know?) (Appendix A).* Type 2 diabetes (T2D), the most common form of diabetes, is often discovered as an insidious disease because it is asymptomatic at the time of screening high-risk patients [1]. Thus, T2D may be detected when a patient attends hospital for surgery, when chronic complications are already present. The main risk is a hyperosmolar hyperglycaemic state when polyuria/glycosuria and hyperglycaemia ($>$ 1.8 g/L or 10 mmol/L) are not compensated for by polydipsia, or parenteral hydration in an unconscious patient. Patients with T2D may require oral antidiabetic drugs (OADs) such as sulphonylureas, which enhance endogenous insulin secretion and may be responsible for hypoglycaemias. Injectable glucagon-like peptide (GLP)-1 receptor agonists, including those that can be injected weekly, reduce the speed at which the stomach empties after a meal, thereby leading to gastroparesis (Appendix B). Insulin may be combined with these drugs.

Type 1 diabetes (T1D) is linked to the autoimmune destruction of pancreatic β cells, which synthesize insulin. The two components for physiological secretion of insulin are then no longer active, namely:

- 'basal' secretion or 'insulin for daily living', which is continuous over the nycthemeral period and represents approximately 50% of daily requirements;
- prandial secretion or 'mealtime insulin'.

Substitution of basal insulin should never be stopped, not even in subjects with euglycaemia, due to the major risk of hyperglycaemia followed by ketosis and diabetic ketoacidosis. In general, patients with T1D are familiar with this rule of survival. Continuous subcutaneous (SC) insulin infusion (CSII) is often used in T1D, as it reproduces basal–bolus delivery through discontinuous SC injections of slow-acting and ultrarapid insulin analogues (Appendix C). Thus, continuous infusion of a small amount of ultrarapid insulin reproduces basal insulin and is the basal output.

'Pancreatic' diabetes secondary to pancreatic disorders is less common, but also presents with severe insulinopenia, with an increased risk of hypoglycaemia because of a simultaneous decrease in glucagon secretion. Other types of diabetes are extremely rare.

*Stress hyperglycaemia and undiagnosed preexisting dysglycaemia.*

*Stress hyperglycaemia.* Surgical procedures and their inherent metabolic effects can induce a stressed state causing perioperative hyperglycaemia, known as 'stress hyperglycaemia'. According to the American Diabetes Association (ADA), this is defined as transient hyperglycaemia in a previously non-diabetic patient during an acute illness or an invasive procedure [1]. It is characterized by plasma glucose levels $\geq$ 1.8 g/L (10 mmol/L), with levels returning to normal ($<$ 1.26 g/L or 7.0 mmol/L) after removal of the stressor and withdrawal of glucose-lowering treatment in patients previously with an HbA1c $<$ 6.5%. The severity of stress hyperglycaemia depends on the type of surgery, invasiveness of the procedure and its duration [2], with the highest prevalence noted during cardiac surgery. Other risk factors include catecholamine infusion, corticosteroid use, obesity, age, hypothermia, hypoxia, cirrhosis, trauma, extensive burns and sepsis [2].

The main mechanism responsible for perioperative stress hyperglycaemia is peripheral insulin resistance with an increase in endogenous glucose production [3]. In addition, renal reabsorption of glucose is increased and/or glucose clearance decreased. Stress hormones (glucagon, cortisol, catecholamines) and mediators of inflammation [interleukin (IL)-1, IL-6] released during surgical stress can lead to perioperative insulin resistance. This affects lipid metabolism with increased release of free fatty acids (FFAs), thus further aggravating insulin resistance [3]. Perioperative insulin resistance may last for several days after an invasive procedure and initially involves insulin-dependent peripheral tissues [3]. Perioperative blood loss as well as prolonged immobilization both affect glucose metabolism in skeletal muscles and accentuate perioperative insulin resistance. In addition, prolonged perioperative fasting induces a decrease in hepatic glycogen supply, and an increase in neoglucogenesis, and lipid and protein metabolism [2].

Hyperglycaemia abolishes ischaemic preconditioning and results in endothelial dysfunction and decreased phagocytic activity of polymorphonuclear neutrophils, while increasing the formation of lesions in a murine blood–brain barrier model of cerebral ischaemia. These deleterious effects of hyperglycaemia are caused by mitochondrial abnormalities in non-insulin-dependent cells, where glucose transporters are overexpressed during stress [2]. The increased release of FFAs is potentially harmful to myocardium as they modify protein metabolism, leading to increased protein catabolism and delayed healing. Insulin therapy mitigates the consequences of insulin resistance, such as the postoperative neurohormonal response to stress and perioperative release of FFAs from peripheral tissues during surgery [2].

*Undiagnosed preexisting dysglycaemia.* The prevalence of undiagnosed T2D is high among hospitalized patients due to age and comorbidities. In a study of 40,836 in-hospital patients (19% with known diabetes), 47% underwent perioperative screening of

plasma glucose levels, which revealed that 18% had plasma glucose levels > 1.8 g/L (10 mmol/L). Hyperglycaemia was observed in 40% of diabetes and 6% of non-diabetes patients [4].

Measurements of HbA1c levels, which reflect glycaemic control over the previous 8–12 weeks, can distinguish patients with unknown diabetes before surgery from those with stress hyperglycaemia [5]. For this reason, HbA1c levels ≥ 6.5% have been used as a diagnostic criterion since 2009 in some countries [1]. The simplest method is to detect undiagnosed dysglycaemia in the preoperative period because:

- prediabetes found during preoperative evaluation indicates a risk for stress hyperglycaemia and its complications;
- complications of undiagnosed diabetes may arise during the perioperative period due to acute glycaemic instability and/or unrecognized chronic diabetes complications.

Thus, these risks should be identified and avoided before surgery whenever possible.

It is proposed that screening be carried out in subjects with signs of diabetes (primary syndrome) or in those at very high-risk for: metabolic syndrome; familial history of diabetes; personal history of cardiovascular events [6]; or history of gestational diabetes mellitus (GDM) or transient hyperglycaemia [7] (Appendix D). Screening by measuring fasting blood glucose [8] and HbA1c levels is also recommended. In fact, such use of HbA1c as a diagnostic criterion for dysglycaemia has already been described in recommendations for the management of patients with acute coronary syndrome [6].

*Evaluating glycaemic control*

Glycaemic control is recommended before hospital admission according to individual targets to avoid hyper- and hypoglycaemia, to monitor glycaemic variability [9] during hospital stays and to improve surgical prognoses (see below). Glycaemic variability is commonly seen due to fasting, stress, the development of infections and use of steroids, for example. Glycaemic control should be evaluated during the visit dedicated to anaesthesia using two criteria:

- HbA1c (chronic control);
- blood glucose (acute control) (Fig. 1).

*HbA1c.* Increased HbA1c in a diabetes patient is associated with high morbidity/mortality and an increased risk of infarction and early postoperative infections [10]. For each 1% increase in HbA1c, the risk increases by 40% [11]. The risk of sternal wound infection is fivefold higher for HbA1c levels > 7.8%. In fact, as HbA1c levels > 7% have a negative prognostic value in unrecognized diabetes patients [12], it is better to postpone a surgical intervention (except in an emergency) if HbA1c is very high (> 9%), as it reflects a lack of glycaemic control, thereby exposing the patient to acute metabolic risks in the perioperative period. On the other hand, HbA1c levels < 5% probably indicate recurrent severe hypoglycaemia in patients treated with insulin or sulphonylurea/glinide, and postponing surgery in such cases is also recommended (Fig. 1). Thus, therapeutic adjustments based on the advice of a general practitioner (GP) or diabetologist should be suggested for HbA1c values between 8% and 9% (chronic but non-life-threatening hyperglycaemia justifies therapeutic reinforcement) and between 5% and 6% (repeated hypoglycaemias justify a reduction of therapy).

*Recent blood and capillary glycaemic values.* There is a correlation between glycaemia at admission (> 2.0 g/L or 11 mmol/L) and postoperative morbidity/mortality [13–15], with a 10-fold greater risk of complications in cases of poor glucose control before surgery [16]. In contrast, blood glucose levels < 1.8 g/L (10 mmol/L) before the intervention lowers the risk of death and infections, and duration of hospital stay [17].

During the preoperative consultation and in the days immediately preceding the intervention, it is necessary to identify recent acute events (hyper- or hypoglycaemia) that might have an effect on perioperative management, with no change in HbA1c:

- hypoglycaemic episodes are the usual consequences of treatment with insulin secretors (sulphonylureas/glinides; Appendix B) or insulin (Appendix C), and are particularly seen in patients with T1D, but also with T2D. The risk is increased in hospitalized patients with diabetes due to more severe glycaemic variability [18], usually defined as plasma glucose levels < 0.7 g/L (3.9 mmol/L). Some hypoglycaemias, however, are not symptomatic, particularly in cases of frequent hypoglycaemias, long diabetes durations and dysautonomia. This is seen in nearly 40% of T1D patients, 10% of insulin-treated T2D patients and occasionally in T2D patients taking sulphonylureas [19];
- episodes of hyperglycaemia and ketosis may be seen in T2D and T1D patients treated with insulin, and the doses and types of insulin should then be modified according to glucose measurements. If necessary, insulin therapy (transient or permanent) may be proposed, particularly if ketosis is detected, before surgery is performed (Fig. 1).

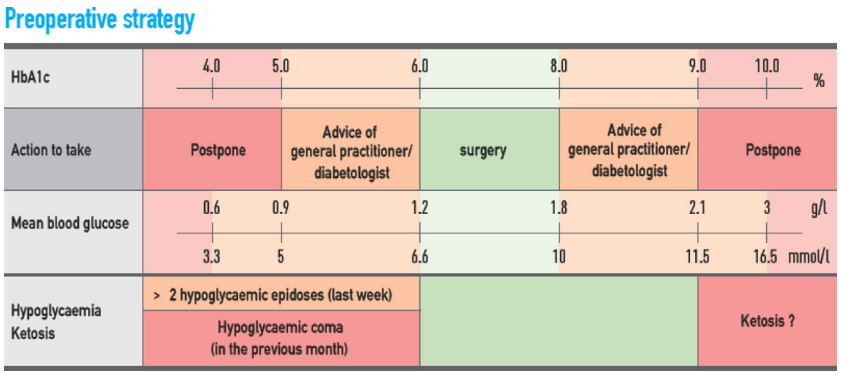


**Fig. 1.** Preoperative management of patients with diabetes: evaluating glycaemic control. D-1: day before surgery; D0: day of surgery; DPP-4: dipeptidyl peptidase 4; GLP-1: glucagon-like peptide 1; SC: subcutaneous; SGLT2: sodium–glucose cotransporter 2; T1D: type 1 diabetes.

*Evaluating specific diabetes complications*

In patients with diabetes, perioperative risk may be increased by the presence of gastroparesis and/or heart disease and/or kidney disease.

*Gastroparesis.* This complication is the most frequent manifestation of digestive dysautonomia, defined as delayed gastric-emptying in the absence of mechanical obstruction. It usually affects diabetes patients with other neuropathic diseases, affecting 30–50% of either T1D or T2D patients. Symptoms classically include anorexia, nausea, vomiting, abdominal pain, sensations of bloating, early satiety and/or slowing of digestion [20]. It may also have adverse effects on the absorption of drugs taken orally. However, there is a weak correlation between symptoms and slowed gastric-emptying; some patients have symptoms without abnormal gastric-emptying. Gastroparesis may be a factor in postprandial glycaemic dysregulation. Furthermore, acute hyperglycaemia can also slow gastric-emptying, thereby suggesting a reciprocal interrelation between gastric-emptying and glycaemia [21]. Clinical examination may reveal abdominal distention with classic slapping of an empty stomach, a late sign of gastroparesis. Oesophageal–gastroduodenal fibroscopy can eliminate other causes of upper digestive tract symptoms and reveal the presence of food remaining in the stomach after overnight fasting. Also, a barium meal may reveal considerable gastric residues or even phytobezoars. The reference diagnostic examination is gastric scintigraphy, using a calibrated, preferably solid meal labelled with technetium 99m [20]. Other tests may be proposed, such as the respiratory test for carbon-13-labelled octanoic acid.

During the anaesthesia consultation, gastroparesis should be investigated because it creates a risk of stasis (full stomach) and inhalation during anaesthesia induction. At the very least, questioning of the diabetes patient during anaesthesia consultation should focus on the classic clinical manifestations of gastroparesis (Fig. 2). If clinical signs suggestive of gastroparesis are present, then measurement of the gastric antrum by echography can distinguish whether the stomach is full or not [22]. Echography can also identify any solid residues. If there is any doubt, 'full-stomach' induction of anaesthesia should be carried out. Erythromycin and metoclopramide, which can help to accelerate gastric motility, may also be used [23,24].

*Cardiac complications of diabetes.*

*Cardiovascular risk with diabetes.* Approximately 75% of diabetes patients die of atherosclerosis complications. However, the degree of cardiovascular (CV) risk is heterogeneous in the diabetes population, as it is linked to coexisting risk factors such as arterial hypertension, lipid abnormalities, smoking and familial history of early CV problems, and to specific factors such as glycaemic control, duration of diabetes and, in particular, the presence of nephropathy. The presence of microalbuminuria is associated with an increased CV risk in both T1D and T2D, and is even greater in the presence of macroproteinuria or renal failure [25]. The presence of arterial damage in any area clearly increases the risk of other arteriopathic damage.

*Heart disease.* This has certain characteristics in diabetes patients; for example, myocardial infarction is often silent, and silent myocardial ischaemia (SMI) is found in 30–50% of asymptomatic T2D patients with no cardiac history except for other CV risk factors [25]. The prognosis for SMI has been demonstrated [26–28], and screening for SMI is based on provocation tests [exercise stress tests with electrocardiography (ECG), myocardial scintigraphy coupled with exercise and/or administration of dipyridamole, stress echography and even stress magnetic resonance imaging (MRI)]. If SMI detection is followed by coronary angiography, the examination can reveal significant coronary stenoses in 30–70% of

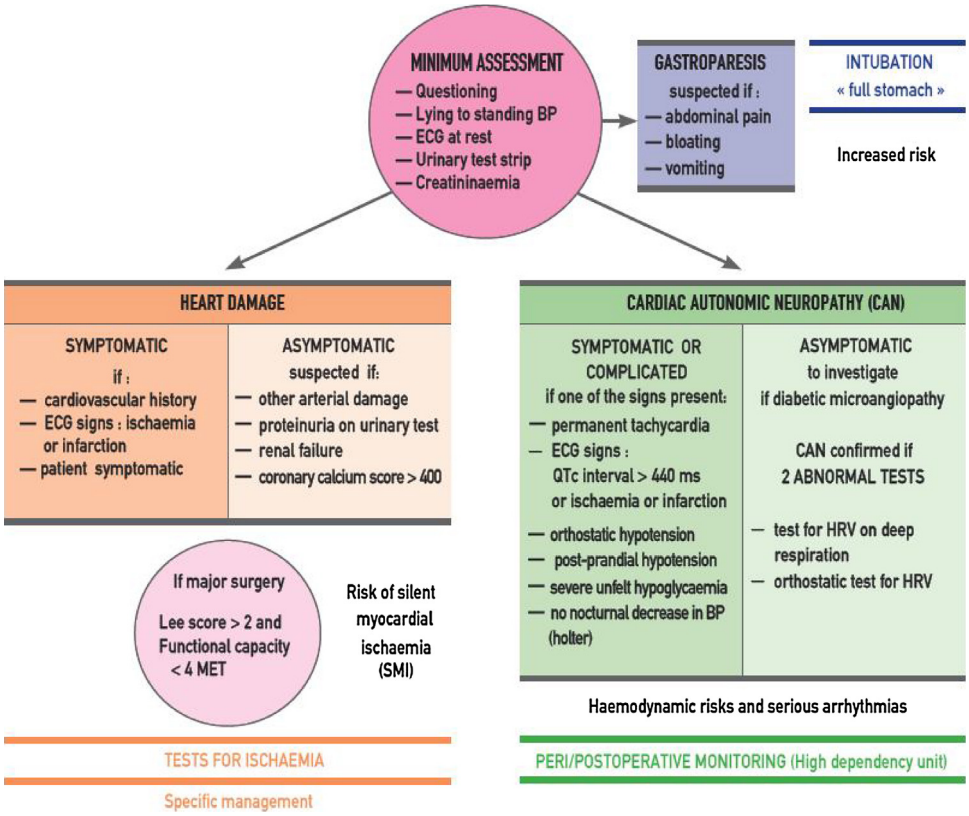


**Fig. 2.** Preoperative management of patients with diabetes: evaluating specific diabetes complications. BP: blood pressure; CAN: cardiac autonomic neuropathy; SMI: silent myocardial ischaemia.

patients with SMI [25]. Detection of heart disease seems logical to prevent cardiac events, but should be reserved for patients at very high CV risk [25]. Measurement of coronary calcium score by cardiac computed tomography (CT; no injection of iodized product) contributes to evaluation of CV risk; a score > 400 Agatston units is associated with a poor prognosis and high prevalence of SMI [29], and should justify investigations for SMI [25]. However, it should be noted that many rigorous studies have shown that systematic coronary revascularization before non-cardiac surgery did not help to reduce complications of postoperative myocardial ischaemia [30]. On the other hand, repeated perioperative measurement of troponin, together with ECG, allowed the detection of perioperative myocardial damage and helped in the initiation of adapted CV treatment [31].

*Heart failure.* The risk of congestive heart failure (HF) is two to three times higher in diabetes patients. Age, duration of diabetes, coronary artery disease (CAD) and the presence of albuminuria are all associated with increased risk of HF [32]. Although CAD and arterial hypertension are the main factors responsible for HF, diabetic cardiomyopathy is a well-established clinical entity and also a proven cause of HF [33]. At the preclinical stage, structural and functional alterations of the left ventricle are frequently observed on echocardiography even in the absence of CAD or hypertension, which is consistent with the presence of diabetic cardiomyopathy. Left ventricular hypertrophy (LVH) is often present, and diastolic or systolic dysfunction may also be detected [34]. Measurement of brain natriuretic peptide (BNP) or pro-BNP levels has good sensitivity for detecting diastolic or systolic dysfunction at the preclinical stage [35].

*Cardiovascular autonomic neuropathy (CAN).* This dysautonomic complication of diabetes is rarely expressed by clinical symptoms, although persistent tachycardia, orthostatic hypotension in particular (often iatrogenic in origin), postprandial hypotension and hypoglycaemia unawareness are symptoms of severe CAN. At the subclinical stage, the most frequent complications of CAN consist of altered heart rate variability (HRV) during standardized tests. Its prevalence increases with duration of diabetes and poor glycaemic control [36]. In one French multicentre study, confirmed or severe CAN, as defined by two or three tests assessing HRV, was present in 20% of patients and significantly associated with the presence of microangiopathic complications [37]. The risks linked to CAN include painless myocardial infarction revealed by systematic ECG, an increase in CV events and an increase in mortality risk, particularly sudden death secondary to severe cardiac rhythm disorders [38,39]. Alterations in ventricular repolarization with prolongation of the corrected QT interval (QTc) on ECG (> 440 ms) and the coexistence of SMI may account for such events [36,39].

Detection of CAN is based on analyses of HRV during standardized tests, including deep-breathing, changes from lying-to-standing and the Valsalva manoeuvre [36]. These tests are usually carried out with a simple ECG and should be interpreted according to age. CAN is then graded according to the results of these tests [36]. However, although relatively easy to perform, these tests take time and require manual calculations, thereby limiting their use in practice outside of a specialized consultation unless a dedicated software programme is used. Changes in HRV can generally, but not specifically, reveal parasympathetic heart damage. The current recommendations suggest carrying out these tests in patients with known T1D of at least 5 years' standing and in all T2D patients, particularly those with microangiopathic complications [40].

If CAN is detected, drugs that might induce orthostatic hypotension should be avoided; the QT interval should be measured by standard ECG (at minimum) and, if prolonged, then a 24-h ECG recording should be performed to detect ventricular ectopic beats [36].

Anaesthesia, whether general or locoregional, has pronounced effects on perioperative sympathetic nervous system (SNS) tone [41]. Several clinical investigations have evaluated the influence of intravenous (IV) anaesthetic agents on muscle SNS activity [41]. However, few studies have evaluated the effects of regional anaesthesia on autonomic nervous system (ANS) tone. Whatever the type of spinal anaesthesia used (spinal block or epidural), the authors reported significant decreases in SNS influx [42,43]. It has also been shown that epidural administration of morphine for operations involving the abdominal aorta decreases postoperative hypertension by reducing sympathetic hyperactivity [44]. In diabetes patients and in cases with metabolic syndrome, peripheral sympathetic activity is enhanced [45]. The interaction between anaesthesia and CAN leads to an increased risk of perioperative haemodynamic instability, although the mechanisms for this are as yet unclear.

Thus, in patients with diabetes, a preoperative decrease in respiratory HRV is associated with risk of perioperative haemodynamic instability [46,47]. Some authors have reported that perioperative requirements for vasopressor support correlate with the degree of perioperative dysautonomia [48,49], which has a long-term postoperative prognostic impact on diabetes patients [48]. Thus, preoperative evaluation of diabetes patients using simple cardiac autonomic function tests (at the very least, for respiratory HRV) appears to be useful for identifying patients at risk of perioperative haemodynamic instability and CV complications despite the absence of clinical symptoms of CAN [36,48]. Diabetes patients with dysautonomia may also have decreased ventilatory responses to hypoxaemia and hypercapnia [50], and to perioperative hypothermia [51]. In such patients, more sophisticated haemodynamic monitoring, including continuous measurement of arterial pressure and cardiac index, may be recommended [52].

*Cardiovascular assessment during anaesthesia consultation.* The modalities of management of coronary patients that should be applied during non-cardiac surgery have been described in the 2011 SFAR/Société française de cardiologie (SFC) recommendations [53]. The present report summarizes the minimum CV and other additional assessments that may be necessary in diabetes patients.

Questioning the patient will determine if: the patient is hypertensive; there is any CV history, in particular, the presence of CAD, heart failure, arrhythmia, cerebrovascular accident or lower-limb vascular disease; the patient is being followed by a cardiologist; the patient has already undergone coronary, supra-aortic or peripheral artery revascularization; there are recent symptoms of angina (mild or atypical) such as dyspnoea or exercise epigastralgia, symptoms evocative of HF or peripheral arteriopathy, symptoms suggestive of orthostatic or postprandial hypotension and/or episodes of asymptomatic severe hypoglycaemia; and/or the patient is taking any current treatment.

The results of earlier investigations are also examined, including the last ECG available, echocardiography, arterial echo-Doppler and investigations for detection of SMI. In addition, a meticulous clinical CV examination is carried out: orthostatic hypotension is assessed and critical ischaemia of the lower limbs is ruled out. A new resting ECG should be performed if the most recent one was carried out several months ago and, depending on the context, signs of ischaemia or even silent infarction, tachycardia, arrhythmia and a prolonged QTc interval should be sought.

Measurements of BNP or pro-BNP levels or echocardiography may be prescribed when HF seems possible. Investigations for SMI are also recommended if a patient scheduled for major surgery has a Lee index score ≥ 2 and a functional capacity < 4 metabolic equivalents of task (METs). The patient should also be referred to a cardiologist for specific management and for tests of ischaemia (Fig. 2).

In patients with no coronary history nor any such symptoms and no specific anomaly on ECG, SMI should be suspected in those at very high CV risk, in particular, the presence of other arterial damage, macroproteinuria, renal failure and a coronary calcium score > 400 Agatston units [25].

When CAN is suspected due to the presence of evocative symptoms or complications (persistent tachycardia, QTc interval > 440 ms, myocardial ischaemia or silent infarction, orthostatic or postprandial hypotension, severe hypoglycaemia unawareness, absence of nocturnal blood pressure decreases), it should be confirmed by tests analyzing HRV. These tests should also look for CAN when microangiopathic complications are present. The proposed procedure includes analysis of HRV during deep-breathing and lying-to-standing tests (Appendix E). The presence of CAN, when confirmed by two abnormal tests or when symptomatic or complicated, should lead to monitoring and peri- and postoperative surveillance in a continuous surveillance unit (Fig. 2).

*Diabetic nephropathy.*

*Epidemiology.* Diabetic nephropathy (DN) affects 30% of patients with T1D and approximately 20% of patients with T2D [54–56]. However, the prevalence of this complication has plateaued or even decreased over the past few years in some countries due to earlier and more appropriate management. In the US, the relative risk of DN has decreased by half (from 13.7% to 6.1%) in 20 years [57]. DN is the most frequent cause of end-stage renal failure, affecting 45% of such cases in the US. In the UK, the mortality rate for diabetes patients aged 18 to 44 years and on dialysis was 30% over 5 years compared with 11% in dialyzed patients without diabetes but with renal failure. Also, renal failure is a major independent risk factor for CV complications, atherosclerosis and insulin resistance, thereby fully justifying its prevention [56,58].

*Diagnosis.* The urinary albumin-to-creatinine ratio (ACR) and glomerular filtration rate (GFR) allow classification of diabetic chronic kidney disease (CKD) [59]. There are three stages of increasing ACR severity, with stage A2 (ACR 30–300 mg/g) corresponding to moderately high albuminuria (previously termed 'microalbuminuria'). It is advisable to measure ACR on one urine sample rather than on 24-h urines, and to perform at least two or three measurements over 6 months to confirm the diagnosis [60]. An estimated GFR (eGFR) is usually based on the Modification of Diet in Renal Disease Study (MDRD) formula (G1–G5), while a decrease in GFR is defined by five stages of increasing severity. Thus, CKD stages G1A1 and G2A1 are considered stable and should prompt annual measurement. For all other stages, the risk of progression to chronic renal failure increases along with CV risk.

*Impact of diabetic chronic kidney disease on anaesthesia.* Diabetes is an independent risk factor for the development of acute renal failure in the perioperative period. This may develop in the absence of previous renal failure or in patients with diabetic CKD. Postoperatively, the presence of diabetic CKD increases the risk [61]. Perioperative evaluation of ACR and GFR is essential during major surgery in emergency cases or if the patient presents with poorly controlled glycaemia. GFR can be estimated using classic formulae if the patient is stable, but should be measured in other situations. The perioperative management of diabetic CKD is non-specific but necessary to avoid administration of nephrotoxic agents or drugs during the perioperative period. Haemodynamic optimalization aims for a mean arterial pressure between 60 and 70 mmHg, and > 70 mmHg if the patient is hypertensive, to maintain renal perfusion pressure. To achieve this objective, haemodynamic monitoring is recommended to evaluate stroke volume as a guide to vascular filling and administration of vasopressors during surgery in cases at risk of haemodynamic instability (haemorrhagic surgery, major or emergency surgery) [61]. All other strategies are non-specific and should follow recommendations for management of acute renal failure [61]. In addition, modalities for administration of anaesthetic agents should take into account the pharmacokinetic and pharmacodynamic modifications resulting from chronic renal failure if this is present with no particular specificity in relation to diabetes.

*Management of treatment, fasting and anaesthesia*

*Managing diabetes treatment. OADs.* Appendix B shows the characteristics of OADs available in France at this time. Metformin is still the first-line therapy for diabetes due to its efficacy in mortality and morbidity [62]. Its use should be considered in patients with moderate renal failure (creatinine clearance 30–60 mL/min) or a history of HF, which are classic contraindications to its use [63]. The most severe risk of metformin is lactic acidosis, with an incidence of 2–9/100,000 patients/year and a mortality rate of 30–50% [64]. Some studies have reported extremely severe cases, but these were always due to the untimely prescription of metformin [65]. It is therefore important to look for risk factors before surgery, including: renal failure (creatinine clearance < 60 mL/min); administration of iodized contrast agents; situations that might alter renal function, such as dehydration, fasting or medical treatment with renin–angiotensin system inhibitors, diuretics and non-steroidal anti-inflammatory drugs; and severe HF (left ventricular ejection fraction < 30%).

In practice, the expert panel recommends:

- stopping metformin the night before;
- not restarting metformin within 48 h of major surgery and only after assuring good renal function;
- continuing metformin in cases of minor or ambulatory surgery except in the presence of severe renal failure (Fig. 1).

Other proposed non-insulin treatments that should not be taken on the morning of minor or major surgery, but continued in cases of ambulatory surgery, are presented in Table 1. Sulphonylureas and glinides may cause hypoglycaemia (Appendix B) and, therefore, taking these medications before emergency surgery indicates that glucose infusion needs to be set up if the patient has an empty stomach. This is not the case with other non-insulin drugs.

*Insulin.* In T1D and because of the risk of ketoacidosis, basal insulin (Appendix C) should never be stopped. The patient's usual basal insulin, whether administered as one or two SC injections or by CSII, should be continued in cases of ambulatory surgery (Fig. 3) or surgery of short duration. Correction of hyperglycaemia during the intervention should be carried out using a corrective bolus, administered by SC injection, of an ultrarapid analogue as per a basal–bolus protocol (Fig. 3).

If CSII is stopped (Appendix F), then long-acting basal insulin should be delivered immediately. This might be 24 international units (IU) of glargine, which acts over 20–24 h (Appendix C) and is necessary if the delivery of insulin outside of meals was 1 IU/h through CSII. The patient should be made aware of this replacement scheme.

*Management of fasting.* If a patient needs to be left with an empty stomach while being treated with insulin, it is recommended to set up a system of glucose infusion (from 0700 h) that never stops if glycaemia is > 16.5 mmol/L. Taking sulphonylureas or glinides before emergency surgery also requires glucose infusion if the patient has an empty stomach. Otherwise, it is not necessary to administer a glucose solution.

*Choice of agents, anaesthetic techniques and intubation.* To date, there is no proof of the superiority of any one anaesthetic agent over another in terms of morbidity/mortality in diabetes patients.

**Table 1**
Preoperative management of patients with diabetes: use of oral antidiabetic drugs (OADs).

| | Ambulatory surgery | Minor or major surgery | Emergency surgery |
|---|---|---|---|
| Metformin | Do not stop | Avoid taking the drug on D-1 (evening) and D0 (morning) | Stop |
| Sulfamides | Do not stop | Avoid taking the drug on D0 (morning) | Stop |
| Glinides | Do not stop | Avoid taking the drug on D0 (morning) | Stop |
| Alpha glucosidase inhibitors | Do not stop | Avoid taking the drug on D0 (morning) | Stop |
| DDP-4 inhibitors | Do not stop | Avoid taking the drug on D0 (morning) | Stop |
| SGLT2 inhibitors | Do not stop | Avoid taking the drug on D0 (morning) | Stop |
| GLP-1 analogues | Do not stop | Avoid taking the drug on D0 (morning) | Stop |
| SC insulin injection | Do not stop | No drug injection on morning of D0 (except for T1D) | Stop |
| Personal insulin pump | Do not stop | Stop the personal insulin pump on arrival in the OR | Stop |

D-1: day before surgery; D0: day of surgery; SC: subcutaneous; T1D: type 1 diabetes.

**Glucose level targeted:** 5 à 10 mmol/L (0.9 - 1.8 g/L)

Diabetes is not a contra-indication to ambulatory surgery

**Pre-anaesthetic consultation**

Search for specific diabetes-induced complications (see Figure 2)
Measurement of HbA1c blood level (see Figure 1)

Patient's care depends on the number of meals skipped

| Number of meals skipped | Time schedule for surgery | What to do? |
|---|---|---|
| 0 | whatever | Continue normal treatment |
| 1 | Before 10 AM | Breakfast and drugs administered after the procedure |
| | Between 10 and 12 AM | No breakfast, drugs given on arrival in the ambulatory unit<br>D10%W infusion maintained until 1st meal if insulin or sulfamide given |
| | After 12 AM | Maintain morning drug administration and light breakfast |
| 2 | *See practical appendix I, J, K* | |

**Preoperative period**

Fasting rules
- Unrestricted dinner on the evening of the preoperative day and drug administration (insulin, oral drugs)
- If personal csii, maintain the csii
- Intravenous line on arrival with D10%W
- Capillary blood glucose on arrival > 16.5 mmol/L (3 g/L): surgery postponed
- Measurement of capillary blood glucose /2H and ultra-rapid insulin analogue according to the following sliding scale

**ULTRA RAPID INSULIN BOLUS SC**
- Capillary blood Glucose/2H
- Ultra-rapid insulin analogue

| | 0,6 | 0,9 | 1,8 | 2,2 | 3 | g/L |
|---|---|---|---|---|---|---|
| | 3,3 | 5 | 10 | 12 | 16,5 | mmol/L |
| 3-9 g glucose IV or sugar 15 g PO | 0 | 0 | 3 | 4 | 6 | IU - SC route<br>+ Ketosis present ? |

**Intraoperative period**
- Capillary blood glucose every hour
- If blood glucose > 10 mmol/L (1.8 g/L):
  - ultra-rapid insulin analogue (see above)
  - if personal csii : no change
  - otherwise start IV insulin infusion

**Postperative period**
- Resume oral intake as soon as possible
- If blood glucose ≤ 10 mmol/L (1.8 g/L): resume preoperative treatment as before (start personal csii if stopped before surgery
- If blood glucose > 10 mmol/L (1.8 g/L): use ultra-rapid insulin analogue boluses as above and delay discharge until capillary blood glucose 5-10 mmol /L
- If blood glucose > 16.5 mmol/L (3 g/L): discharge contra-indicated and hospital admission for IV insulin infusion

**Fig. 3.** Management of patients undergoing ambulatory surgery. D10%W: 10% dextrose in water; IV: intravenous.

In fact, general anaesthesia and regional anaesthesia (RA) give similar results in such patients, although RA is associated with a slight increase in glycaemia preoperatively. While spinal block and epidural anaesthesia can help to limit hyperglycaemic severity, they expose the patient to haemodynamic risk. The choice between general anaesthesia and RA is made as for any other patients.

While peripheral nerve blocks are not contraindicated in diabetes patients [66], they should only be carried out after

analyzing patients' records and taking several precautions that are more important in these patients than in non-diabetes patients, including preoperative clinical examination for signs of dysautonomia (see above) and preexisting polyneuropathy to gain more precise information on the given patient.

In addition, the conditions for intubation should be clearly specified, as intubation may be difficult due to densification of periarticular collagen structures in the temporomandibular and atlanto-occipital joints. As these metabolic collagen disorders (non-enzymatic glycosylation, anomalies of metabolism) simultaneously affect the interphalangeal joints, it is generally advisable to evaluate the potential difficulties of tracheal intubation with a palm-print test in patients with long-term diabetes.

### *Perioperative period*

#### *Prognosis of perioperative hyperglycaemia*

*Relationship between hyperglycaemia and complications.* Most studies have been conducted during cardiac surgery or in intensive care units (ICUs). Perioperative hyperglycaemia is an independent risk factor of postoperative morbidity and mortality [67,68], although maximum perioperative glycaemia is associated with perioperative morbidity and mortality [16,67,69,70], with a 10-fold higher risk of complications when postoperative glycaemia is > 2.5 g/L (13.5 mmol/L) [16]. An increase in glycaemia of 0.2 g/L (1.1 mmol/L) above 1 g/L (5.5 mmol/L) increases this risk by 34% [70]. In cardiac surgery, there is an increase in sternal wound infections in patients with mean preoperative glycaemia > 2.0 g/L (11 mmol/L) [17] whereas, in non-cardiac surgery, a prospective study in which 20% of patients had diabetes also found a relationship between glycaemia and infections [71]. In patients with undiagnosed diabetes, hyperglycaemia was associated with an increased risk of infection, repeat interventions and in-hospital mortality [72].

The prognosis for hyperglycaemia appears to differ depending on whether it is stress hyperglycaemia or poor glycaemic control in patients with diabetes. In a cohort of patients undergoing non-cardiac surgery, the glycaemic threshold above which mortality was significantly increased was different depending on whether the patient had diabetes (1.8 g/L or 10 mmol/L) or not (1.4 g/L or 7.8 mmol/L) [73].

Nevertheless, the prognostic impact of perioperative hyperglycaemia justifies its early detection by performing regular measurements of glycaemia and its correction, particularly in at-risk surgical patients (aged > 60 years, presence of a metabolic syndrome, previous history of transitory hyperglycaemia, CV history).

*Better glycaemic control and prognosis: observational studies.* In 14,051 aortocoronary bypass patients studied between 1987 and 2001, management of hyperglycaemia in the perioperative period in those with diabetes was shown to decrease mortality by 57%, reaching the level of non-diabetes patients [68]. Mean serum glucose levels fell to 1.77 g/L (9.73 mmol/L) compared with 2.14 g/L (11.8 mmol/L) in the historical group. Similar results were found in retrospective studies where the incidence of mediastinitis and mortality decreased by 37% and 29%, respectively, in groups with a glycaemic target of < 2.0 g/L (11 mmol/L) [72,73]. An initial meta-analysis carried out in 2004 reported a 15% decrease in mortality in ICUs when glycaemia was controlled by insulin therapy [74]. Furthermore, retrospective studies comparing different blood glucose levels demonstrated that patients with glycaemia in the range of 1.26–1.79 g/L (7–10 mmol/L) had better prognoses than those with glycaemia < 1.26 g/L (7.0 mmol/L) during aortocoronary bypass [14] as well as with fewer hypoglycaemic episodes [15].

*Better glycaemic control and prognosis: randomized interventional studies.* In one randomized study, a significant decrease in infections at the cardiac surgical site (0% vs. 13%, respectively; $P < 0.01$) was reported in the treated (glycaemic target 1.2–1.8 g/L or 6.6–10 mmol/L) vs. untreated (glycaemic target < 2.5 g/L or 13.7 mmol/L) groups [13]. In 2001, van den Berghe et al. [75] published the first randomized study (1558 patients in surgical ICUs: 60% with cardiac surgery, 13% with diabetes) to compare a strict-target (0.8–1.0 g/L or 4.4–5.5 mmol/L) vs. a conventional target (1.8–2.0 g/L or 10–11 mmol/L), and demonstrated an 8% decrease in mortality and a decrease in morbidity (including septicaemia and duration of antibiotic therapy) in the intensive (strict-target) group. In contrast, the multicentre randomized Normoglycemia in Intensive Care Evaluation and Surviving Using Glucose Algorithm Regulation (NICE-SUGAR) study [76], carried out in 6104 patients in surgical and medical ICUs (20% diabetes patients) and comparing strict vs. conventional glycaemic targets, showed no benefit in terms of morbidity. In fact, mortality as well as the number of severe hypoglycaemic events increased (+2.8%) in those receiving intensive vs. conventional treatment, with mean blood glucose levels of 1.15 g/L (6.3 mmol/L) vs. 1.44 g/L (8.0 mmol/L), respectively. In 2008, a meta-analysis of the largest randomized studies concluded not only that there was no benefit with intensive management in ICUs, but also that there was an increased risk of hypoglycaemia [77].

Nevertheless, it should be pointed out that, in the most recent randomized studies (the NICE-SUGAR in particular), the group receiving conventional treatment had mean blood glucose levels that were clearly < 2.0 g/L (11 mmol/L). Thus, while intensive treatment was not superior to conventional treatment, it did enable blood glucose levels to be maintained at < 1.8 g/L (10 mmol/L), levels that in older studies were demonstrated to benefit morbidity/mortality.

In addition, in a randomized study of 300 patients undergoing aortocoronary bypass, Umpierrez et al. [78] compared different glycaemic targets, including strict (1.1–1.4 g/L or 6.0–7.7 mmol/L) and moderate (1.4–1.8 g/L or 7.7–10 mmol/L) control of glycaemia. No differences in morbidity, sternal wound infection rates, mortality or duration of hospital stay were found, although hypoglycaemic episodes were more frequent in those receiving intensive treatment.

In general, hyperglycaemia (> 1.8 g/L or 10 mmol/L) in the perioperative period increases morbidity/mortality and, therefore, control of glycaemia should start in the preoperative period and be continued into the early postoperative days. However, while patients benefit more from a reduction in glycaemia than from insulin therapy, targeting normoglycaemia (0.8–1.2 g/L or 4.4–6.7 mmol/L) increases the rate of severe hypoglycaemia and possibly mortality as well. Thus, moderate glycaemic control (1.4–1.8 g/L or 7.7–10 mmol/L) appears to be the best compromise, resulting in a decrease in morbidity/mortality without increasing the frequency of hypoglycaemia. However, maintaining stable blood glucose levels at 1.4–1.8 g/L or 7.7–10 mmol/L requires complex insulin protocols that are difficult to implement without a computer programme. Thus, a more realistic target is to maintain glycaemia at 0.9–1.8 g/L (5–10 mmol/L), with the latter value being the threshold above which therapeutic adjustment is called for.

#### *Perioperative management of glycaemia*

Fig. 4 shows the general principles of intravenous insulin infusion (IVII), which should be applied immediately before and during surgery. If the patient has been using CSII, it should be stopped and replaced with mandatory immediate IVII at the beginning of the intervention; in this case, the hourly infusion rate may be similar as that of CSII. Ultrarapid short-acting analogues

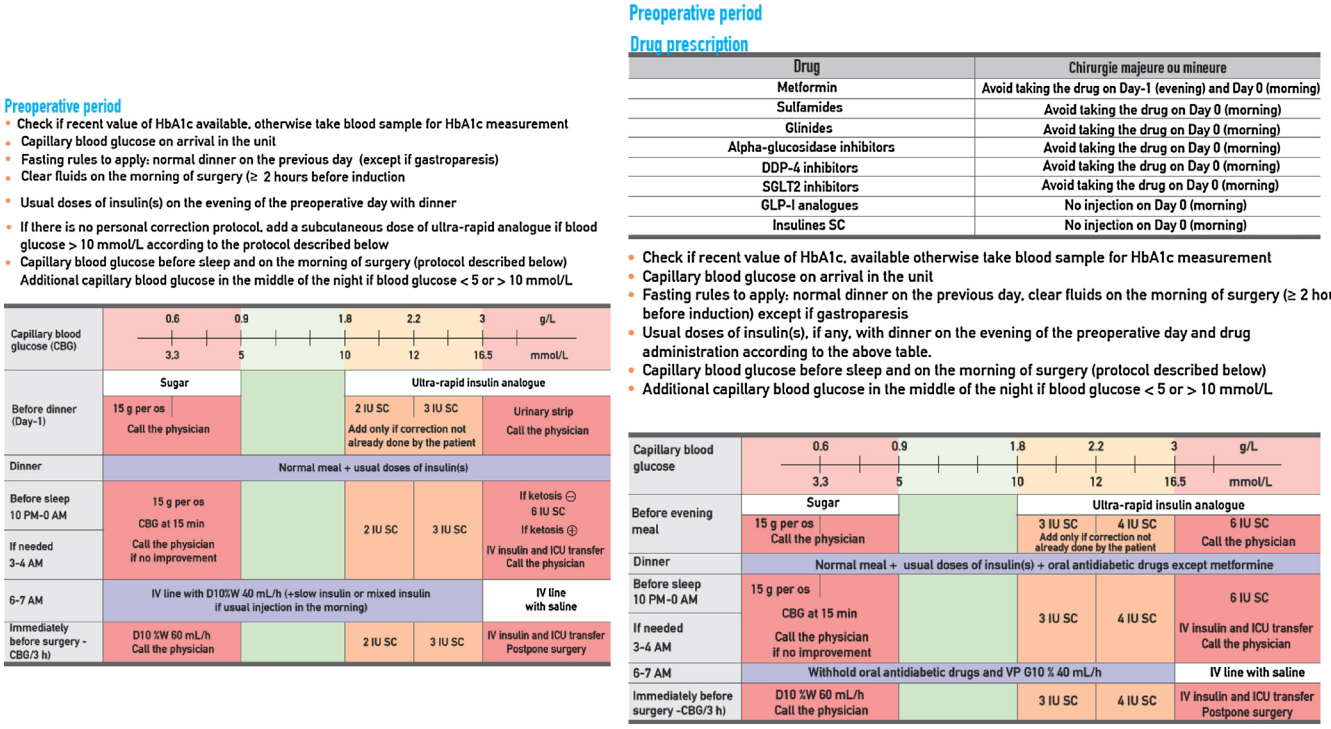


**Fig. 4.** Glycaemic management of patients with type 1 and type 2 diabetes just before surgery. CBG: capillary blood glucose; D10%W: 10% dextrose in water; ICU: intensive care unit; IU: international unit(s); IV: intravenous; SC: subcutaneous.

(Appendix C) should be preferred for IVII, which should always be given in association with IV glucose (equivalent to 4 g/h), plus electrolytes if especially needed to avoid insulin-induced hypokalaemia. All solutes may be used in the perioperative period, including Ringer's lactate.

Fig. 5 shows the protocol for IVII during surgery. Prolonged fasting should be avoided and the diabetes patient should be scheduled for surgery as early in the morning as possible. The dogma of prolonged preoperative fasting has recently been called into question by several studies reporting beneficial effects by administering preoperative carbohydrates (enterally or parenterally) on postoperative insulin resistance in non-diabetes patients [79].

Glycaemia should be monitored every 1–2 h, and kalaemia controlled by insulin every 4 h in the perioperative period. Measurements should be carried out using arterial or venous blood and a blood gas analyzer rather than with capillary blood and glucose meters. Indeed, glucose meters overestimate glycaemia, especially in cases of vasoconstriction and hypoglycaemia [80]. Thus, a value of 0.7 g/L (3.8 mmol/L) on a glucose meter should be considered hypoglycaemia and followed by corrective action after checking the value by measurement in a laboratory. Hypoglycaemias are especially frequent in the perioperative period, most likely due to the prolonged fasting and/or irregular food intake. Deterioration of renal or hepatic function, or the use of quinolones, heparin, β-blockers or trimethoprim–sulphamethoxazole may further increase the risk.

*Other elements of management*

*Prophylaxis for nausea and vomiting.* Prevention of nausea and vomiting is an essential part of the perioperative strategy, especially in diabetes patients, given the importance of rapid resumption of eating. In this context, it is valid to propose an anaesthetic strategy that minimizes the risk of nausea/vomiting. However, of the more powerful antiemetics validated for use in the perioperative period, dexamethasone carries the risk of hyperglycaemia: although an 8-mg dose is considered more antiemetic than a 4-mg dose [81], it exposes the patient to a greater risk of hyperglycaemia. Thus, our recommendation is to use 4 mg of dexamethasone in combination with another antiemetic, such as droperidol or a 5-HT3 antagonist.

*Treatment of pain.* Poorly controlled pain is a risk factor for hyperglycaemia. The usual analgesics do not affect glycaemic control and can be used with no modification of indication or dose. In patients with diabetes, those with poor glycaemic control have higher analgesic needs than those with HbA1c levels < 6.5% [82]. The use of RA should be favoured whenever possible, as they are associated with better control of postoperative pain.

*Other measures.* Modulation of perioperative insulin resistance is a major therapeutic goal as it helps to significantly reduce the duration of postoperative hospital stays [79]. Prevention of hypothermia, use of RA and multimodal analgesia (to enable more rapid resumption of bowel movements), limitation of blood loss, early ambulation and minimally invasive surgery are all preferred measures. Also, diabetes does not alter the usual rules for antibiotic prophylaxis.

*Postoperative period*

*Immediate postoperative glucose control*

*Change from IVII to SC insulin.* The basal–bolus scheme is the most suitable for the postoperative period, taking into account the variable nutritional supply and insulin requirements. The most widely used model to ensure transition from IVII to subcutaneous (SC) insulin is that of Avanzini et al. [83] (Fig. 6). The changeover is made when blood glucose levels are stable for at least 24 h and eating has resumed. In general, half the total dose of IV insulin corresponds to a dose of long-acting insulin, while the other half equates to doses of three preprandial ultrarapid analogues. Some teams recommend giving 80% of the IV insulin dose as slow-acting

- Use ultra-rapid insulin only, diluting it to a concentration of 1 IU/mL.
- Always include simultaneous glucose infusion (100-150 g/day) except if hyperglycaemia > 16.5 mmol/L (3 g/L). Example: D10 % W: 40 mL/h.
- Perioperative glycaemic objectives: 5 mmol/L -10 mmol/L (0.9 -1.8 g/L).
- Administer a direct IV loading bolus depending on starting blood glucose level then maintain by IV insulin infusion.
- Measure blood glucose level every 2 h if stable glycaemia, every hour after each change of insulin flow rate and after 15-30 min in the case of hypoglycaemia.
- Adapt IV insulin infusion flow rate depending on glycaemic control according to the following scheme:

| Glycaemia | | 0.4 g/L / 2.2 mmol/L | 0.6 / 3.3 | 0.9 / 5 | 1.1 / 6 | | 1.8 / 10 | 2.5 / 14 | 3 / 16.5 |
|---|---|---|---|---|---|---|---|---|---|
| Initiation IV insulin infusion | IV Bolus | 0 | 0 | 0 | 0 | | 3 IU | 4 IU | 6 IU |
| | IV insulin infusion flow rate | 0 | 0 | 0 | 1 IU/h for T1D<br>0 IU/h for T2D | | 2 IU/h | 3 IU/h | 4 IU<br>Inform clinician |
| Frequency of blood glucose measurement | | 15 min | 30 min | 1 h | 1 h | 2 h | 1 h | 1 h | 1 h |
| Adaptation of insulin infusion flow rate | | Stop<br>Resume at 1/2 rate when :<br>- glyc. > 5 mmol/L in T1D<br>- glyc. > 10 mmol/L in T2D | Stop | - 1 IU/h | - 1 IU/h | idem | + 1 IU/h | + 2 IU/h | Bolus 6 IU<br>Inform clinician |
| D30 % W | | 2 amp. (6 g)<br>Inform clinician | 1 amp. (3 g) | | | | | | |

- Prefer measurement of glycaemia in whole blood (arterial or venous taken from the opposite side to the glucose infusion) rather than capillary blood and if possible use a blood gas machine (rather than a glycaemia test strip)
- Monitoring of potassium blood concentration : objective 4-4.5 mmol/L. Measure every 4 h if concentration is stable and 1 h after each change of insulin flow rate.

**Fig. 5.** Protocol for intravenous (IV) insulin infusion during surgery. Amp: ampoule; D10%W/D30%W: 10%/30% dextrose in water; T1D/T2D: type 1/type 2 diabetes; IU: international unit(s).

insulin and adding the first dose of ultrarapid insulin to the first meal [84]. However, Lazar [85] consider it necessary to wait until the rate of infusion is < 3 IU/h before starting the follow-up, as faster speed comes with an excess risk of postoperative complications.

If IVII is given over a short period of time (< 24 h) in patients not previously treated with insulin and whose blood glucose levels remain increased postoperatively, it is advisable to start insulin at a daily dose of 0.5–1.0 IU/kg weight (half long-acting insulin, half ultrarapid analogue) and to give only half the anticipated dose of ultrarapid analogue if the meal is light [86]. In fact, the Working Group has also made some general recommendations (Fig. 6). A patient usually using CSII should be reconnected in the postoperative period as soon as the patient can manage autonomously (Appendix F). If the patient is not autonomous, it is mandatory to initiate a basal–bolus scheme using SC insulin.

*Management of hypoglycaemia.* Monitoring of blood glucose levels should be continued postoperatively to detect hypoglycaemia; otherwise, the management strategy is identical to that of the perioperative period. Sampling should be performed not only when faced with any symptoms suggestive of hypoglycaemia, but also regularly in case of hypoglycaemia unawareness. Faced with hypoglycaemia < 3.3 mmol/L (0.6 g/L), glucose should be administered immediately even in the absence of clinical signs. Likewise, glucose administration is recommended for blood glucose levels of 0.7–1.0 g/L (3.8–5.5 mmol/L) if the patient reports signs of hypoglycaemia. The oral route should be preferred when the patient is conscious whereas, if a subject is unconscious or not able to swallow, then IV glucose should be administered immediately and oral glucose administered when the patient regains consciousness (Appendix G).

*Management of hyperglycaemia.* Severe hyperglycaemia (notably ketoacidosis, hyperosmolarity) should be investigated by postoperative monitoring of blood glucose levels (Appendix H). In cases of hyperglycaemia > 3.0 g/L (16.5 mmol/L) in T1D and T2D patients treated with insulin, the presence of ketosis should be systematically investigated. In the absence of ketosis, the addition of an ultrarapid insulin analogue and hydration should be rapidly initiated. If ketosis is present, then the initial stages of ketoacidosis should be suspected, a physician called and the administration of an ultrarapid insulin analogue started (transfer to an ICU should also be discussed).

In patients with T2D, severe hyperglycaemia may also suggest diabetic hyperosmolarity ('hyperosmolar coma'), the clinical manifestations of which are extremely variable and deceptive (asthenia, moderate confusion, dehydration). Blood electrolytes should immediately be measured to confirm hyperosmolarity

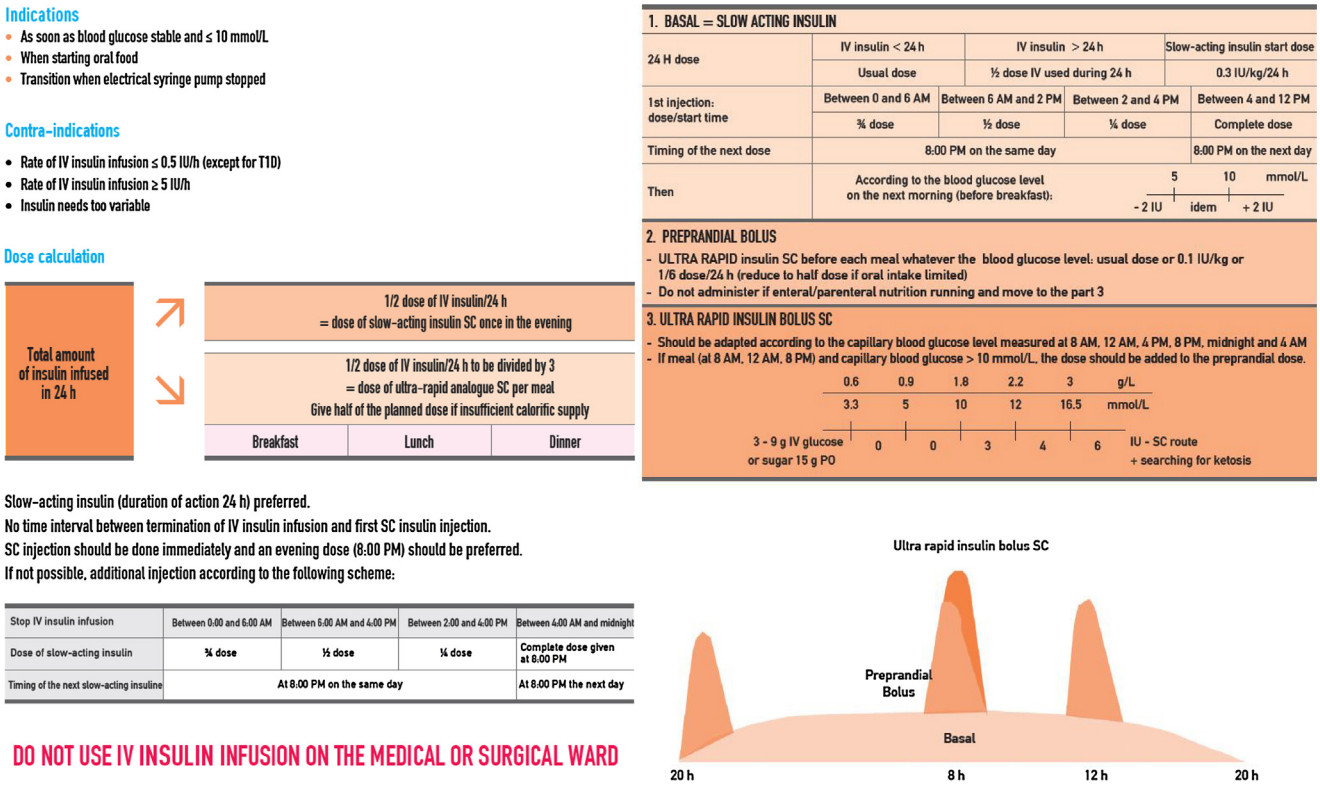


**Fig. 6.** Calculation of dose for transition from intravenous insulin infusion (IVII) to subcutaneous (SC) insulin. IU: international unit(s).

(> 320 mOsmol/L) and prompt specific management in an ICU. Except for a life-threatening emergency, ketosis and hyperosmolarity should lead to postponement of surgery.

*Glucose-lowering treatment just before discharge.* Patients' treatment and follow-up are adapted according to a personalized HbA1c target [62], usually around 7%, and postoperative care depends on the patients' glucose control, type of diabetes and usual treatment. Thus, care is conditioned by three parameters: type of diabetes; its treatment; and preoperative glycaemic control after minor or major surgery.

*Patients with T1D.* In T1D, resumption of previous treatment combining basal (long-acting) insulin and bolus (ultrarapid analogue) insulin is essential (Appendix I). Patients are discharged with their usual insulin regimens, but with dosages as administered in hospital. Specific consultations can be arranged with a diabetologist before discharge in cases of HbA1c > 9% or if glycaemic control is not achieved (> 2.0 g/L or 11 mmol/L), or after discharge if HbA1c levels are 8–9%.

*Patients with T2D taking OADs alone.* When HbA1c is ≤ 8%, previous OAD treatment is resumed at the same doses after 48 h (if creatinine clearance is > 30 mL/min for all OADs or > 60 mL/min for metformin). Ultrarapid insulin doses are progressively tapered until they can be stopped. The patient's GP is consulted within 1 or 2 weeks. When HbA1c is 8–9%, OADs are resumed at the same doses if there is no contraindication, ultrarapid insulin is stopped, but long-acting insulin is continued. Nurse support is suggested at home to adapt insulin doses. The GP is consulted the following month and a future consultation with a diabetologist is arranged.

However, when HbA1c remains > 9% and/or glycaemic control is not achieved (blood glucose > 2.0 g/L or 11 mmol/L), the basal–bolus scheme is continued and the advice of a diabetologist is requested before discharge (Appendix J).

*T2D treated with OADs and insulin before hospitalization.* The proposed procedures for patients with T2D treated with insulin preoperatively are the same progressive strategies as for T1D. When HbA1c is < 8%, the previous treatment is resumed at the same dosages as used in hospital. When HbA1c is 8–9%, the previous treatment is resumed, but consultation with a diabetologist is requested for intensification of therapy. When HbA1c is > 9% or glycaemic control is not achieved (blood glucose levels > 2.0 g/L or 11 mmol/L), the basal–bolus scheme is continued and the advice of a diabetologist is requested (Appendix K).

*Stress hyperglycaemia.* Stress hyperglycaemia is characterized by hyperglycaemia despite an HbA1c < 6.5%. Insulin is progressively stopped, depending on capillary blood glucose levels. No treatment is necessary on discharge from hospital, although monitoring is essential as 60% of these patients will become diabetic within a year, according to Greci et al. [87]. Fasting blood glucose should be measured after 1 month, then annually and/or systematically in all stress situations. The patient's GPs should also be informed.

*Diabetes patients with previously unknown disease.* While dietary recommendations are made by a dietitian, the advice of a diabetologist should be requested before the possible initiation of an OAD, with consultation with a GP at 1 month. Patients' education is crucial for better glycaemic control [88,89], fewer subsequent hospitalizations [88,89], lower risks of ketoacidosis and nosocomial infections, and shorter hospital stays [90]. Support from a mobile diabetes team is also welcome.

## *Specific situations*

### *Ambulatory surgery*

*Organization.* In 2014, ambulatory surgery represented approximately 45% of surgical procedures in France (http://www.

chirurgie-ambulatoire.org/fr/flambee-taux-chir-ambu). Selection of patients for such surgery traditionally considers two main factors:

- the nature of the procedure (minor surgery);
- the underlying health status and comorbidities.

Nowadays, ambulatory surgery is also available to diabetes patients (http://sfar.org/prise-en-charge-anesthesique-des-patients-en-hospitalisation-ambulatoire/), albeit with tight organizational and technical approaches to minimize the risk of poor glycaemic control and to allow patients to return to their previous lives more quickly. Many diabetes patients (notably those with T1D) know how to effectively manage their own blood glucose levels at home postoperatively.

However, only one recommendation [91] and two studies evaluating practices for diabetes patients undergoing ambulatory surgery have been published over the past 5 years [92,93]. In general, the aim is to maintain adequate glycaemic control and avoid hypoglycaemia. It is logical to minimize any changes to OAD and insulin treatment, to resume normal eating as soon as possible and to regularly monitor blood glucose levels. According to DiNardo et al. [92], the anaesthesiologist is the most competent person to guide patients' management and make the necessary changes to treatment. The main elements are summarized in Fig. 3.

Preoperative evaluation is the same as for any hospitalized patient (Figs. 1 and 2). Criteria that could lead to surgery being declined or temporarily postponed depend on the indication and on glycaemic control. Knowing the result of a recent HbA1c measurement will also help to define a strategy (Fig. 1). Treatment should not be modified (unless a longer hospital stay than usual is necessary or the patient does not immediately resume eating), and metformin should not to be taken the evening before surgery (Fig. 3). No specific premedication is required.

As for the perioperative strategy, patients take their usual treatments and eat as usual the evening before surgery. On admission to the ambulatory surgery unit, a peripheral venous line is inserted, although glucose infusion is only necessary if resumption of normal eating is delayed (see below). Care may be regulated according to the number of meals the patient has to skip.

In the majority of cases, a single meal (the morning of admission) is skipped. The patient may, however, drink clear fluids before hospital admission. If the operation is short and the patient is transferred to the discharge room [after leaving the post-anaesthesia care unit (PACU)] before 1000 h in the morning, then breakfast is served and the patient can take the morning medication at that time. Priority should therefore be given to diabetes patients on the surgical list. If a patient expects to leave the PACU between 1000–1200 h, he/she should not take the usual medication in the morning before going to hospital, but take it on arrival at hospital. Glucose infusion should then be set up (10% glucose at 40 mL/h) and continued until the next meal if treatment includes insulin or an insulin-secreting drug (sulphonylurea or glinide; Appendix B). If the patient is scheduled to leave the PACU even later (after 2400 h), a light breakfast (including solids) should be eaten and medication taken before departing for hospital. A peripheral venous line may be inserted, but glucose infusion may not be necessary. Finally, if surgery and anaesthesia are scheduled so that the patient does not skip a meal, treatment should continue and the patient should have breakfast as usual.

*Glycaemic control.* Capillary blood glucose levels are measured on arrival at the ambulatory surgery unit. A glycaemic target of 0.9–1.8 g/L (5–10 mmol/L) is recommended. An insulin (ultrarapid analogue) bolus is administered if capillary blood glucose is $>$ 1.8 g/L or 10 mmol/L (Fig. 3). During the procedure, blood glucose is measured hourly, especially if the operation is long.

If blood glucose is $>$ 3.0 g/L (16.5 mmol/L), surgery should be postponed and treatment with a corrective bolus administered, with blood glucose measurement every 2 h. If such treatment leads to rapid control of blood glucose, then surgery can be carried out. However, if glycaemic imbalance persists with blood glucose $>$ 3.0 g/L (16.5 mmol/L), the patient should be admitted to hospital and IVII initiated.

*Postoperative period.* Oral feeding should be resumed as soon as possible and repeated measurement of blood glucose continued. If blood glucose levels are $\leq$ 1.8 g/L (10 mmol/L), then regular treatment is resumed at the usual times. If blood glucose levels are $>$ 1.8 g/L (10 mmol/L), the patient should remain in hospital and receive intermittent injections of corrective SC boluses until glucose falls to 0.9–1.8 g/L (5–10 mmol/L). Finally, if blood glucose levels are $>$ 3.0 g/L (16.5 mmol/L), then going home is contraindicated and the patient should be admitted to hospital to initiate IVII.

*Pregnancy and diabetes*

*Definition.* During pregnancy, it is necessary to distinguish between known preexisting diabetes and GDM. T2D is now more common than T1D in pregnant women. These two types of diabetes are treated with insulin during pregnancy, possibly with CSII (60% of T1D, 10% of T2D). In women with T1D, there is a risk of ketosis, or even ketoacidosis, even when blood glucose levels are only moderately elevated [94]. Screening for ketosis should therefore be carried out if there are clinical signs despite blood glucose levels $<$ 2.0 g/L (11 mmol/L), due to the risk of fetal death in the absence of treatment.

*Risk of neonatal hypoglycaemia during delivery.* For neonates, the risk of hypoglycaemia (10–40%) is greater if their mothers had poor glycaemic control during both pregnancy and labour [95–97]. This risk is even higher when infants are born of a mother with T1D, when neonates have macrosomia or in cases of prematurity. The consequences, mainly neurological, are related to their duration and severity.

*Glycaemic targets during labour and delivery.* During labour, these targets are determined in relation to risk of neonatal hypoglycaemia. The SFD recommends aiming for blood glucose levels close to normal [98]. Nevertheless, neonatal hypoglycaemia may still arise even when maternal blood glucose levels are controlled during labour. In a retrospective study of 197 women with T1D, there was a significant negative correlation between neonatal and maternal blood glucose levels only when the latter were $>$ 1.44 g/L (8 mmol/L) [97]. Thus, the same glycaemic objectives as described by Lepercq et al. [96] are here proposed: maternal blood glucose levels at 0.8–1.4 g/L (4.4–8.25 mmol/L).

*Actions to be taken.* Fig. 7 describes the steps to be taken in the three types of diabetes (T1D, T2D, GDM) at three different stages of childbirth concerning insulin treatment:

- during dilation of the cervix, treatment for each type of diabetes is continued as during pregnancy with the same glycaemic objectives;
- during delivery, insulin therapy may be either stopped or continued. In patients with T1D or T2D and in those with GDM and blood glucose levels $>$ 1.4 g/L (8.25 mmol/L), IVII should replace insulin injections during labour or caesarean section, and be continued until their return to the PACU (Appendix L). In cases of GDM, IVII should only be used if the glycaemic objective is not achieved (glycaemia $>$ 1.4 g/L or 8.25 mmol/L). In women

**Glucose level targeted: 4.4 mmol/L – 7.8 mmol/L (0.8 g/L – 1.4 g/L)**

| At the time of delivery | T1D | T2D known or discovered during pregnancy | Gestational diabetes (with or without insulin) |
|---|---|---|---|
| Cervical ripening | Maintain insulin treatment unchanged, usual daily doses | | |
| | Risk of ketoacidosis if personal insulin pump stopped or basal insulin withdrawn | | |
| Labour room | D10%W and IV insulin | D10%W and IV insulin | D10%W and IV insulin if blood glucose > 7.8 mmol/L (1.4 g/L) |
| | If personal insulin pump stopped: transition to IV insulin (or the patient may prefer maintaining the personal pump)<br>If caesarean delivery: maintain IV insulin until discharge from PACU | | |
| Immediately after delivery | See liaison form (Diabetologist/Maternity unit/Patient) | | |
| Transition SC insulin – IV insulin | - If continuous subcutaneous insulin infusion (csii) : start immediately when stopping the insulin infusion<br>- If once-daily basal injection<br>o Immediate SC injection of last dose given > 24 H ago<br>o Or at the usual administration time if last dose < 24 h ago<br>- If twice-daily basal injection<br>o Immediate SC injection of last dose given > 12 h ago<br>o Or at the usual administration time if last dose < 12 h ago | - Resume treatment with subcutaneous insulin according to medical prescription | No |
| Postpartum use of insulin | Use liaison form (Diabetologist/Maternity unit/ Patient)<br>Or use insulin 80 % of dose used before pregnancy<br>Or use insulin 50 % of dose used at the end of pregnancy | | No |
| Capillary blood glucose | Before meals (target < 1.5 g/L) and before sleep (target < 1.8 g/L) | | Before meals (target < 1.1 g/L) |
| Advice from a diabetologist | Yes | Yes | |

**Fig. 7.** Diabetes and pregnancy. D10%W: 10% dextrose in water; IV: intravenous; PACU: post-anaesthesia care unit; T1D/T2D: type 1/type 2 diabetes.

using CSII, it is preferable to switch to IVII as CSII during labour would require a personalized protocol to adapt CSII output. Glucose infusion is necessary in cases of insulin therapy (Appendices L, N), as labour is a state requiring the consumption of energy during the active phase, during expulsion and when labour is extended. Thus, patients treated with insulin require a 10% glucose infusion to avoid maternal hypoglycaemia and ketosis brought on by fasting;

- as the immediate postpartum period depends on the type of diabetes, anticipation is recommended, with a planned protocol using a liaison form filled in by a diabetologist (Appendix M). After labour, glycaemic objectives are not as strict, with a proposed range of 1.1–1.6 g/L (6.0–8.8 mmol/L) after vaginal delivery or slightly lower after caesarean section, to support wound-healing [94]. If such a protocol is not defined, then the following principles for diabetes management would apply:
  - in T1D patients, resume the basal–bolus insulin regimen, but at a decreased dose (either 80% of the dose used before pregnancy or 50% of the dose at the end of pregnancy). As long-acting insulin should be continuous, when IVII is stopped, long-acting insulin should immediately be resumed if the last injection was administered > 24 h earlier (if once a

day). If the patient is using CSII, it should be restarted as soon as IVII is stopped. T1D patients are usually autonomous in the management of their diabetes,
- in insulin-treated T2D patients, insulin is continued at half-dose while awaiting the advice of a diabetologist,
- in GDM cases, insulin is stopped while monitoring of blood glucose before and 2 h after a meal is continued for 48 h. Treatment should be discussed with a diabetologist if fasting blood glucose levels are > 1.26 g/L (7 mmol/L) and postprandial blood glucose levels are > 2.0 g/L (11 mmol/L; Fig. 7).

*Paediatric patients*

Children and adolescents occasionally require minor or major surgery. In such cases, the appropriate management of diabetes is crucial to avoid acute metabolic complications (severe hypoglycaemia, ketosis with or without acidosis) and to provide optimal postoperative outcomes. The International Society for Pediatric and Adolescent Diabetes (ISPAD) recently updated its clinical practice consensus guidelines for the management of children and adolescents with diabetes requiring surgery [99].

*Diabetes in children.* Children and adolescents with diabetes mostly have T1D (> 90%). T2D is uncommon, but increases among obese adolescents, especially those of non-Caucasian ethnicity, and often requires insulin therapy during puberty. In France, almost half of our paediatric patients use CSII [100]. Patients using injections are mostly on a basal–bolus regimen, although some are still using conventional therapy. Treatment adaptations need to be managed by patients' parents, especially in unusual situations such as sick days and during intense physical activities. Glycaemic variability is usually highly pronounced in children, as very young children are not able to recognize signs of hypoglycaemia. Ketosis is also not unusual, especially in very young children in a fasting state and in all diabetes patients with insulin deficiency. For these reasons, whenever possible, surgery in children and adolescents with diabetes should be performed at centres with appropriate staff and facilities to care for such patients. Insulin therapy should never be discontinued, not even for a short period of time, and glycaemic values should be monitored closely with targets adapted to a paediatric population [99].

*Specific recommendations for surgery.* Children and adolescents with T1D or T2D treated with insulin need to be admitted to hospital if general anaesthesia is required. Switching to IVII with glucose infusion is imperative for major surgery (lasting > 2 h) or in patients treated with intermediate-acting insulin (Appendix C) to avoid hyperglycaemia and ketosis, and to promote safe fasting. Also, any specific adjustments should be planned by both the anaesthesiologist and paediatric endocrinologist, taking into consideration the type of surgery, insulin regimen and time of the procedure.

Careful blood glucose monitoring (hourly) is crucial during and after surgery as well as ketone testing. Glucose targets are usually set in the range of 5.0–6.6 to 10 mmol/L. In cases of hypoglycaemia, 30% dextrose should be infused and IVII reduced, but never stopped, to avoid ketosis.

*Ambulatory setting.* If the expected duration of surgery is short (< 2 h) in a patient using basal–bolus therapy (injections or pump therapy), an ambulatory setting may be proposed. The patient should be scheduled as the first case of the day to avoid prolonged fasting and risk of ketosis. For patients using an insulin pump, a switch to basal insulin the night before may be necessary if the anaesthesiology team is not accustomed to manipulating insulin pumps.

*Patients at risk of diabetes.* Some children who have, for example, cystic fibrosis or are transplant recipients are at risk of dysglycaemia in the surgical setting. Thus, it is recommended that such patients undergo preoperative evaluation of glucose metabolism (fasting blood glucose, HbA1c) if possible, with monitoring of capillary blood glucose during and soon after surgery. Also, ketoacidosis in children may sometimes mimic an abdominal surgical emergency. For this reason, glucose values should be checked before any operation to eliminate prior polyuria, polypnoea, ketone breath or unexplained hyponatraemia.

*Urgent surgery*

Our recommendations in such emergency cases (summarized in Appendix N) are to measure HbA1c levels and, without waiting for results, to stop any treatment with OADs or insulin injections, and to replace CSII by IVII (Fig. 5).

*Role of diabetologists*

Several studies have highlighted the benefits of referring patients to a diabetologist in the perioperative period (before, during and after hospitalization), as such a consultation offers an opportunity to optimalize treatment as well as initiate, update or complete patients' education about their diabetes.

In the preoperative period, the GP or anaesthesiologist should seek the advice of a diabetologist if diabetes is diagnosed just before surgery or, if diabetes is known, the patient has poor glycaemic control: frequent or asymptomatic hypoglycaemic episodes (HbA1c < 5%); mean blood glucose level > 1.8 g/L (10 mmol/L); or HbA1c > 8%. Intensification of treatment would then be necessary to improve glycaemic control and reduce the risk of surgical complications.

Also, during the stay in hospital, management by a diabetologist appears to be beneficial in terms of better glycaemic control [101], fewer recurrent hospitalizations for diabetes [101,102], shorter stays in hospital [102] and lower healthcare costs [102]. In a previous study, Levetan et al. [103] showed that, in patients hospitalized for reasons other than diabetes, consultation with a diabetologist reduced the mean duration of hospital stay from 8.2 days to 5.5 days. Referral to a diabetologist during hospitalization is also recommended if blood glucose is > 2.0 g/L (11 mmol/L) or HbA1c is > 9% or treatment was not adapted (Appendices I–K). In addition, the use of point-of-care glucose meters may be of interest in this setting.

Overall, referring a patient to a diabetologist is recommended in the following cases:

- known diabetes with poor preoperative glycaemic control (HbA1c < 5% or > 8%);
- diabetes diagnosed during hospitalization or anaesthesia consultation;
- diabetes with poor glycaemic control during hospitalization (HbA1c > 9%) or inadequate previous treatment;
- blood glucose > 3 g/L (16.5 mmol/L) during ambulatory surgery;
- after a diabetes patient with HbA1c > 8% has been discharged from hospital.

## Conclusion

Several strategies to maintain target-range glucose values perioperatively have been proposed here. The goals of perioperative diabetes management include avoidance of hypoglycaemia, prevention of ketoacidosis, maintenance of fluid and electrolyte balance, and avoidance of marked hyperglycaemia. During surgical

procedures and in the postoperative phase, the aim is to maintain glucose in the range of 1.4–1.8 g/L.

Ideally, all patients with diabetes should undergo surgery before 0900 h in the morning to minimize disruption of their treatment routine. For short procedures, patients with T2D treated by diet alone may not require any therapy perioperatively, although supplemental fast-acting insulin analogues may be given to patients whose glucose levels rise over target. Patients with T2D treated with OADs or non-insulin SC drugs are advised to take their usual treatment in the morning before surgery. Insulin may be given as correction or for meals.

Patients with T1D should continue with SC insulin perioperatively, but at a reduced dose for procedures that are not long and complex (no more than one or two skipped meals). However, for long and complex procedures (such as coronary artery bypass graft), IVII is usually required.

In addition, the working group emphasizes the need for anaesthesiologists to be trained in the perioperative management of patients with diabetes and to work in collaboration with diabetologists.

## Disclosure of interest

The authors declare that they have no competing interest.

## Appendix A. Supplementary data

Supplementary data (Appendices A to N) associated with this article can be found, in the online version, at https://doi.org/10.1016/j.diabet.2018.01.014.

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