Diabetes and adult surgical inpatients

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Key points

Diabetes mellitus (DM) is the most common metabolic disorder and patients often present for surgery.

Drug therapy for DM has expanded in recent years and knowledge of newer drugs and insulin formulations is essential for safe management of diabetic patients.

Complications of DM include cardiovascular, renal, and neurological and affect anaesthetic management. Meticulous preoperative assessment is essential.

Choice of anaesthetic technique should be made on an individual patient basis. Intraoperative blood glucose control and frequent measurement of blood glucose and serum potassium are key to safe practice.

Postoperative care includes adequate analgesia, treatment of postoperative nausea and vomiting, and a return to the patient's normal diabetic regimen as soon as possible.

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Epidemiology

Diabetes mellitus (DM) is the most common metabolic disorder, and in the UK, 4–5% of the population are diabetic. The prevalence is expected to increase rapidly over the next decade as a consequence of obesity, lack of exercise, increased migration of susceptible patients, and an ageing population. Type 2 diabetes accounts for ~90% of the patients with DM. As the prevalence of DM increases so the number of diabetic patients requiring surgery will increase. Surgery is often undertaken for the complications of DM such as peripheral vascular disease, coronary artery disease, and renal failure but diabetes may be unrelated to the surgical procedure. The duration of hospital stay was found to be greater in diabetic patients compared with non-diabetic patients particularly after orthopaedic and plastic surgery.[1]

Diagnosis

The diagnosis of DM is based on fasting plasma venous glucose concentrations and plasma glucose values after a 75 g oral glucose load (Table 1).[2] The latter, an oral glucose tolerance test (OGTT), is not used for routine diagnostic purposes because of its inconvenience, greater cost, and poor reproducibility. The OGTT is undertaken when the diagnostic category is uncertain. Three abnormal criteria are defined: impaired fasting glucose, impaired glucose tolerance, and DM. Impaired fasting glucose and impaired glucose tolerance are clinically important as 5–10% of these individuals develop DM each year.

Complications

Most of the increased mortality and morbidity found with DM results from the micro- and macrovascular complications. Risk factors for the complications of DM include: long duration of diabetes, poor glycaemic control, obesity, hypertension, hyperlipidaemia, smoking, and a sedentary lifestyle.

Microvascular complications

Diabetic nephropathy has become the commonest cause of renal failure in the developed world and progresses through several well-defined stages. Persistent albuminuria should be treated vigorously with good glycaemic control and management of associated hypertension and hyperlipidaemia. Angiotensin-converting enzyme-inhibitors or angiotensin receptor blocking agents are effective in slowing the progression of renal disease. Diabetic patients who develop end-stage renal disease have worse outcomes on dialysis and transplantation than non-diabetic patients with greater cardiovascular morbidity and mortality.

Diabetic retinopathy and nephropathy are closely associated. Retinopathy also progresses through well-defined stages with end-stages of a proliferative retinopathy with the risk of retinal detachment and vitreous haemorrhage and macular oedema.

Diabetic neuropathy includes generalized and focal changes. The most common generalized neuropathy is a mixed sensory and motor polyneuropathy which usually presents as a peripheral sensory polyneuropathy alone. The combination of peripheral vascular disease and a sensory neuropathy often results in critical ischaemia in the leg. A diabetic autonomic neuropathy is found in ~50% type 1 diabetics and 20% type 2 diabetics.[3] The resultant cardiac dysfunction and gastroparesis are of obvious anaesthetic relevance. Focal neuropathies include carpal tunnel syndrome, third cranial nerve palsies, and diabetic amyotrophy.

Macrovascular complications

Diabetes confers about a two-fold excess risk for a wide range of vascular diseases, independent of other risk factors.[4] Cardiovascular disease accounts for ~75% of all deaths in type 2 diabetics, but the association of type 1 diabetes is less clear. Risk factors for cardiovascular disease in type 1 diabetics include the presence of a nephropathy, autonomic neuropathy, hypertension, hyperlipidaemia, and

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Table 1 Diagnosis of DM

Criteria	Fasting plasma venous glucose (mmol litre^{-1})
Diabetes mellitus	Fasting $\geq$7.0 2 h post-glucose load $\geq$11.1
Impaired glucose tolerance	Fasting $<$7.0 2 h post-glucose load $>$7.8 and $<$11.1
Impaired fasting glucose	Fasting $\geq$6.1 and $<$7.0 2 h post-glucose load $<$7.8
Glucose load is 75 g orally	

Table 2 Drugs used to treat DM. GLP-1 agonists, glucagon-like peptide-1; DPP-4, dipeptidyl peptidase-4 inhibitors

Sulphonylureas
Biguanides
Thiazolidinediones
GLP-1 receptor agonists
DPP-4 inhibitors
Amylin analogues
Meglitinides
α-Glucosidase inhibitors
Insulin

microvascular cardiac disease. The benefits from good glycaemic control in preventing macrovascular disease are unclear in type 1 diabetics. Coronary artery disease, cerebrovascular disease, and hypertension occur commonly in type 2 diabetics. There is considerable evidence to show that intensive treatment of hypertension, nephropathy, and hyperlipidaemia, together with good glycaemic control, decreases the risk of vascular complications in type 2 diabetics.[5]

Drug therapy

The currently available classes of drugs used to treat DM are shown in Table 2. Of particular interest at present are the thiazolidinediones (TZDs), glucagon-like peptide-1 (GLP-1) receptor agonists, dipeptidyl peptidase-4 (DPP-4) inhibitors, and new formulations of insulin (for a detailed review of all drugs, see Nicholson).[6]

Thiazolidinediones

These compounds enhance insulin sensitivity, lower HbA_{1C} by 1–2%, and decrease fasting and postprandial glucose concentrations. They do not cause hypoglycaemia when given alone but can do so when used in combination with other agents. TZDs can cause oedema, weight gain, and worsen cardiac failure; they are contraindicated in patients with liver disease and New York Heart Association class III or IV cardiac status. The use of rosiglitazone was associated with a significantly increased risk of death from cardiovascular disease, so this drug is not recommended for use in type 2 diabetics. Pioglitazone is relegated to third-line treatment only.

GLP-1 agonists

Incretins are gut-derived peptides secreted in response to meals. A major incretin is GLP-1 which is released from the ileum and colon, enhances insulin secretion from the pancreas, suppresses glucagon release, delays gastric emptying, and suppresses appetite. An i.v. infusion of GLP-1 increases circulating insulin values even in patients with longstanding type 2 diabetes. Unfortunately, GLP-1 is of limited use clinically as it is rapidly degraded by DPP-4. Synthetic analogues, exenatide and liraglutide, have been developed that are resistant to breakdown by DPP-4. Both compounds are given daily (liraglutide) or twice daily (exenatide) by s.c. injection, but a weekly formulation of exenatide has been developed recently.[7] Exenatide is cleared by the kidneys, but liraglutide is not excreted by this route. GLP-1 agonists decrease fasting and postprandial glucose concentrations, HbA_{1C} by 1–2%, and weight by 2–5 kg. Gastrointestinal side-effects, nausea, vomiting, and diarrhoea, occur particularly when starting therapy.

DPP-4 inhibitors

These compounds enhance the effects of endogenous GLP-1 by inhibiting the action of the enzyme DPP-4. The drugs are given orally once a day; saxagliptin, sitagliptin, and vildagliptin are currently available. They have similar effects on circulating glucose and HbA_{1C} as the GLP-1 agonists, but do not suppress appetite or result in weight loss. The DPP-4 inhibitors can be used as monotherapy, are well tolerated with a low risk of hypoglycaemia, and cause less gastrointestinal side-effects than the GLP-1 agonists.

Insulin

The goal for insulin therapy is to mimic the physiological pattern of secretion found in normal individuals; basal release to sustain low circulating values in the starved state with rapid release in response to meals. The development of rapidly acting insulin analogues such as insulin aspart, insulin glulisine, and insulin lispro together with long-acting analogues insulin glargine and insulin detemir has enabled many insulin-dependent diabetics to adopt this 'basal-bolus' regimen. The long-acting insulin is given daily and the short-acting insulin injected 15–30 min before meals. Insulin glargine and insulin detemir provide a constant release of insulin from the injection site over 24 h. Continuation of the long-acting insulin (basal) throughout the perioperative period is logical and has been adopted in some centres.

Preoperative assessment

Key points in preoperative evaluation are shown in Table 3. The type, duration, and current treatment of DM must be ascertained and a recent HbA_{1C} estimation shows the adequacy of glycaemic control in the previous 2–3 months. High preoperative HbA_{1C} values (>8–9%) have been shown to be associated with adverse outcomes after a variety of surgical procedures.[8] Overt

Table 3 Basic preoperative evaluation of diabetic surgical patients

Diabetes	Type
	Duration
	Treatment
Cardiovascular disease	Coronary artery disease
	Peripheral vascular disease
	Hypertension
	Cerebrovascular disease
Renal disease	
Peripheral neuropathy and possibly autonomic neuropathy	
Metabolic control, HbA_{1C}	
Airway, cervical spine, stiff joint syndrome	
Drugs and allergies	

cardiovascular disease is common in diabetic patients and should be investigated as indicated clinically and the current therapy noted carefully. It is sensible to manage all longstanding diabetic patients as if they are at high risk of perioperative myocardial ischaemia.

Important microvascular complications for the anaesthetist are diabetic nephropathy and neuropathy. The presence of albuminuria, and the amount excreted per 24 h, indicates the onset and severity of a nephropathy. Circulating creatinine concentrations should be measured before operation in all diabetic patients. In patients in whom regional anaesthesia (RA) is used, the presence and extent of a peripheral neuropathy should be determined. Although there is no evidence that the neuropathy is exacerbated by neural blockade, recent studies have suggested that the peripheral nerves in diabetic patients may be more susceptible to trauma and local anaesthetic toxicity.[9] Patients with an autonomic neuropathy may be asymptomatic but the occurrence of a resting tachycardia, orthostatic hypotension, constipation/diarrhoea, gustatory sweating, and impotence are strongly suggestive of autonomic dysfunction. Testing for an autonomic neuropathy before operation is not routine and it is usually assessed by determining heart rate variability. Variability is lost with autonomic neuropathy.

Assessment of the airway is particularly important in type 1 diabetic patients as they can develop the stiff joint syndrome with limited mobility of the upper cervical spine resulting in difficult tracheal intubation. Since these patients may also have an autonomic neuropathy with gastroparesis, they are at a particular risk of regurgitation and aspiration.

Preoperative investigations are determined by the findings of the history and examination. The following basic investigations should be undertaken in all diabetic patients: blood glucose concentration, urinalysis for albumin and ketones, haemoglobin, blood urea, creatinine, and electrolytes, and ECG. Further investigations are determined clinically.

Metabolic management

Control of blood glucose in the surgical diabetic patient is complicated by several factors. Preoperative starvation should be minimized, and after surgery, the early resumption of oral intake enables the diabetic patient to return to their usual treatment regimen. The prevention and prompt treatment, if necessary, of postoperative nausea and vomiting is a vital part of perioperative care. The endocrine and metabolic response to surgery further complicates glucose control. Catabolic hormone secretion increases blood glucose, and in diabetic patients with no or impaired endogenous insulin, there are no metabolic constraints on the hyperglycaemic effects of these hormones. Anaesthetic drugs may influence the glucose response to surgery in diabetic patients by decreasing catabolic hormone secretion (RA and opioids) or inhibiting any residual insulin secretion (volatile anaesthetics).

The aims of metabolic management are to avoid hypoglycaemia, excessive hyperglycaemia, and to minimize lipolysis and proteolysis by the provision of exogenous glucose and insulin as necessary.

Target blood glucose concentration

Studies of the potential benefits of glucose control in diabetic surgical patients have been triggered by the plethora of studies in critically ill patients in the past decade. In cardiac surgery, there is evidence to suggest that intraoperative and postoperative control of blood glucose with insulin in diabetics and non-diabetics improved morbidity, particularly the incidence of postoperative wound infections.[10] At present, there are few studies examining the effects of glucose control in diabetic patients undergoing general surgery. In most trials in which 'strict' glucose control (<6.1 mmol litre^{-1}) was implemented, hypoglycaemia was a common hazard. The anaesthetist is left to decide on safe glucose limits for the diabetic patient with no clinical evidence to guide this decision for most surgical patients. It is reasonable to suggest that blood glucose should be maintained between 6 and 10 mmol litre^{-1} which was a recommendation of the American Association of Clinical Endocrinologists and the American Diabetes Association in 2009.[11]

Glucose control type 1 diabetics

It has been a usual practice to manage all type 1 diabetic surgical inpatients with a glucose–insulin–potassium (GIK) regimen. The infusion is started as soon as possible after admission on the morning of surgery and continued for at least 1 h after the first meal to prevent rebound hyperglycaemia. The Alberti regimen, a premixed bag of glucose 10%+insulin+potassium, has been largely superceded by separate infusions of insulin (soluble insulin 50 units in 50 ml) and glucose 5% or 10% with or without potassium at 100–120 ml h^{-1}. The infusions must join before the i.v. cannula and a non-return valve must be used. This variable rate insulin infusion is flexible and easily changed to achieve the target glucose concentration but does not have the inherent safety of the Alberti regimen. The key to success with the separate glucose and insulin infusions is to maintain a constant infusion of insulin.

Table 4 RA for diabetic patients

Disadvantages	Advantages
Neuraxial block	Awake patient
Increased cardiovascular instability with diabetic autonomic neuropathy	Avoids tracheal intubation
Increased risk of infection	May decrease catabolic hormone response
	Good postoperative care
Peripheral block	
Exacerbation of neuropathy by direct damage	
Increased local anaesthetic toxicity	

Repeatedly discontinuing the insulin infusion results in poor glucose control.

Diabetic patients using the 'basal-bolus' regimen may not need a GIK regimen if the overall period of starvation, preoperative and postoperative, is short. The 'basal' insulin will provide a continuous release of insulin which is unlikely to result in hypoglycaemia if the perioperative fast is similar in duration to the patient's usual overnight fast. 'Bolus' insulin is given when eating restarts. This strategy has been successful in ambulatory surgery.

Glucose control type 2 diabetics

Type 2 diabetics treated with insulin should be managed similarly to type 1 diabetics (see above). Type 2 diabetics treated with drugs other than insulin should have these omitted on the day of surgery. Those undergoing major surgery almost invariably need a GIK regimen and the insulin requirements are often large because of insulin resistance. The management of 'moderate' surgery is contentious. It has been suggested that the use of a GIK regimen results in greater metabolic problems than careful monitoring with glucose/insulin as required. The decision can only be made on an individual patient basis.

There has been concern that the use of metformin after surgery may increase the risk of lactic acidosis if nephrotoxic agents are given (particularly radio-opaque contrast). In diabetic patients with normal serum creatinine values, an estimated glomerular filtration rate of >50 ml min^{-1} or both, metformin may be resumed immediately.[12]

Anaesthesia

There is no evidence that RA improves mortality and morbidity after major surgery in diabetics compared with general anaesthesia. The disadvantages and advantages of RA are shown in Table 4, and the risk–benefit profile must be considered for each patient.

The prolonged administration of a GIK infusion results in hyponatraemia as the glucose is metabolized to leave excess free water. Additional i.v. fluids can be 0.9% sodium chloride of Hartmann's solution, but in elderly patients receiving 100–125 ml h^{-1} GIK regimen, there is a risk of fluid overload. The infusion of 50% glucose decreases markedly the volume of glucose solution required, but this must be given slowly into a central vein. At present, there is not readily available an ideal crystalloid solution for infusion into diabetic patients perioperatively. The adoption of a solution of 0.45% sodium chloride with 5% glucose and 0.15% potassium chloride has several advantages. Red cell concentrates are stored in saline–adenine–glucose–mannitol at a glucose concentration of 0.9% (50 mmol litre^{-1}). The infusion of several packs of red cells is an important additional glucose load.

Monitoring metabolism

The key to successfully managing diabetic patients is the frequent measurement of blood glucose with appropriate changes in insulin, glucose administration, or both as required. During, and immediately after, major surgery, glucose should be measured hourly. This interval can be lengthened to 2 and then 4 h when stable glucose values have been achieved. Plasma potassium concentrations should be measured on alternate glucose samples.

It is important to be aware of possible inaccuracies in the measurement of glucose with strip assays. The FDA permits a $\pm 20\%$ error for glucose meters at values ≥ 5.5 mmol litre^{-1} and assay strips tend to overestimate values at low concentrations. Many factors can affect the measurement: hypoperfusion, anaemia, increased circulating bilirubin and uric acid, mannitol, dopamine, dextran, and paracetamol.[13]

Postoperative care

Before discharge to the ward, appropriate analgesia, treatment for nausea and vomiting, and i.v. fluids should be prescribed. Good postoperative analgesia, particularly RA, decreases catabolic hormone secretion which aids glucose control. Non-steroidal anti-inflammatory drugs must be used with great caution as they may further impair renal function in patients with a nephropathy. Prophylaxis against nausea and vomiting should have been undertaken during surgery but must be treated vigorously if it occurs. Dexamethasone exacerbates insulin resistance and is best avoided. The anaesthetist should ensure that the blood glucose is within the target range, that the circulating potassium concentration is normal, and that an appropriate variable rate insulin infusion, if required, has been prescribed before the patient is released to the ward.

Conflict of interest

None declared.

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Please see multiple choice questions 29–32.