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.

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...
Glucose load is 75 g orally.

Impaired fasting glucose
Fasting, 6.1–7.0

Impaired glucose tolerance
2 h post-glucose load, >7.0 and <11.1

Diabetes mellitus
Fasting, ≥7.0
2 h post-glucose load, >11.1

Table 1 Diagnosis of DM

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Fasting plasma venous glucose (mmol litre⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>≥7.0</td>
</tr>
<tr>
<td>Impaired glucose tolerance</td>
<td>≥7.0</td>
</tr>
<tr>
<td>Impaired fasting glucose</td>
<td>≥6.1 and &lt;7.0</td>
</tr>
<tr>
<td>Glucose load is 75 g orally</td>
<td></td>
</tr>
</tbody>
</table>

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

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

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

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 HbA1c 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 subcutaneous 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, HbA1c 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 HbA1c 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 HbA1c estimation shows the adequacy of glycaemic control in the previous 2–3 months. High preoperative HbA1c values (>8–9%) have been shown to be associated with adverse outcomes after a variety of surgical procedures.8 Overt...
Contact the history and examination. The following basic investigations
should be undertaken in all diabetic patients: blood glucose con-
centration, urinalysis for albumin and ketones, haemoglobin, blood
electrolytes, and ECG. Further investigations
can be performed as indicated clinically.

Peripheral neuropathy and possibly autonomic neuropathy
Metabolic control, HbA1C
Airway, cervical spine, stiff joint syndrome
Drugs and allergies

Cardiovascular disease
Renal disease

**Metabolic management**

Control of blood glucose in the surgical diabetic patient is compli-
cated by several factors. Preoperative starvation should be mini-
mized, 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 inhib-
iting any residual insulin secretion (volatile anaesthetics).

The aims of metabolic management are to avoid hypoglycaemia,
excessive hyperglycaemia, and to minimize lipolysis and prote-
olysis 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 infec-
tions. At present, there are few studies examining the effects of
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 inhib-
iting any residual insulin secretion (volatile anaesthetics).

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excessive hyperglycaemia, and to minimize lipolysis and prote-
olysis by the provision of exogenous glucose and insulin as
necessary.

**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 superseded by separate infusions of insulin (soluble insulin
50 units in 50 ml) and glucose 5% or 10% with or without potas-
sium 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.

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**Table 3** Basic preoperative evaluation of diabetic surgical patients

<table>
<thead>
<tr>
<th>Diabetes</th>
<th>Type</th>
<th>Duration</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease</td>
<td>Coronary artery disease</td>
<td>Peripheral vascular disease</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Renal disease</td>
<td>Peripheral neuropathy and possibly autonomic neuropathy</td>
<td>Metabolic control, HbA1C</td>
<td>Airway, cervical spine, stiff joint syndrome</td>
</tr>
</tbody>
</table>
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 ±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.

**References**


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**Table 4 RA for diabetic patients**

<table>
<thead>
<tr>
<th>Disadvantages</th>
<th>Advantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuraxial block</td>
<td>Awake patient</td>
</tr>
<tr>
<td>Increased cardiovascular instability with diabetic autonomic neuropathy</td>
<td>Avoids tracheal intubation</td>
</tr>
<tr>
<td>Increased risk of infection</td>
<td>May decrease catabolic hormone response</td>
</tr>
<tr>
<td>Peripheral block</td>
<td>Good postoperative care</td>
</tr>
<tr>
<td>Exacerbation of neuropathy by direct damage</td>
<td></td>
</tr>
<tr>
<td>Increased local anaesthetic toxicity</td>
<td></td>
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</tbody>
</table>

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Please see multiple choice questions 29–32.