The liver is the only mammalian organ that can regenerate functionally active parenchyma after tissue loss. Exploitation of this physiological property has allowed for the liver resection surgery to develop, and it is now a commonly performed procedure. During the 1970s, perioperative mortality for hepatic resection was quoted around 20%, commonly because of uncontrollable bleeding and postoperative liver failure. Improvements in the understanding of liver anatomy, patient selection, and also surgical and anaesthetic techniques have contributed to a reduction in quoted perioperative mortality to around 3%,1 although patients with parenchymal liver disease (e.g. cirrhosis) have significantly higher rates of complications and mortality.

**Indications**

Hepatic resection is now the treatment of choice for colorectal hepatic metastases without evidence of more distant disease spread, and remains the commonest indication for liver resection in the UK. Five-year survival is negligible in un-treated patients compared with around 30%1 in those receiving hepatic resection. The liver resection is also used in the management of benign and malignant primary hepatobiliary tumours, donation for transplantation, and occasionally in hepatic trauma.

**Liver anatomy**

The liver is highly vascular, receiving a total blood flow of ~1.5 litre min⁻¹, of which 80% is supplied by the portal vein and 20% from the hepatic artery. The liver can be divided into five sectors and further sub-divided into eight functional segments (Fig. 1), described by their blood supply and biliary drainage. The portal vein divides successively to supply each liver segment, reflecting similar divisions of the hepatic artery and bile duct. Segmental portal and hepatic arterial blood supply and biliary drainage are unique, so contiguous segments can be resected without disrupting the vascular supply to neighbouring tissue. There are few bloodless planes of dissection, and functional divisions are invisible on the surface of the liver.

**Regeneration**

Liver regeneration occurs by hyperplasia of the remnant. Mature hepatocytes replicate within 24 h of resection, followed by increase in cell size. Non-parenchymal cells such as bile-duct, endothelial and Kupffer cells have a slower replication process. The overall regeneration process after hepatic resection, diabetes mellitus, and ischaemic or toxic insults, is slower in older patients. Liver regeneration is also seen after occlusion of branches of the portal vein. Techniques employing pre-resection ligation or embolization of the selective portal vein supplying the diseased liver segments have been developed to increase the size of the post-resection remnant and increase resectability.

**Surgical technique**

The surgical aim is to excise the diseased part of the liver with adequate oncological clearance, minimal blood loss, and leaving enough healthy liver to avoid liver failure and allow regeneration. Laparoscopic procedures are far less common than open procedures, but are recognized by NICE for liver cysts, peripheral solitary metastases and hepatocellular carcinoma. Often an additional incision is used (hand assisted) with the aid of a gas tight sleeve.

The surgical procedure can be divided into three main phases: initial, resection, and confirmation of haemostasis and wound closure.

**Initial phase**

The liver is mobilized from peritoneal attachments, cholecystectomy is performed and, if indicated, vascular anatomy is exposed.
Resection

Before operation, exact tumour location and vascular anatomy may be confirmed with CT (also used to exclude extra-hepatic spread) and MRI (100% sensitive for lesions >1 cm) examinations, allowing planning of the surgical approach. The resection may require lobectomy, remove entire functional segments, or involve atypical wedge resection. Intra-operative ultrasound is mandatory to confirm preoperative assessments and identify additional lesions.

Parenchymal transection has been described using a number of techniques. Commonly, dissection with a clamp crushing technique or Cavitron Ultrasonic Aspirator (CUSA) are used to disrupt liver parenchyma, revealing vessels and bile ducts that may then be clipped or ligated.

Blood loss is significantly reduced using temporary occlusion of the blood supply to the liver during parenchymal resection. This may involve total inflow occlusion of the portal vein and hepatic artery (Pringle manoeuvre). The resulting decrease in cardiac output of up to 10% and increase in left ventricular afterload of 20–30% may cause cardiovascular compromise. Segmental vessels can also be identified and selectively occluded, causing less cardiovascular disturbance. Very occasionally, total hepatic vascular occlusion is required to access tumours close to the vena cava, which involves clamping of the supra and infra-hepatic vena cava and also the hepatic pedicle. However, this technique is associated significant haemodynamic compromise, with reductions in cardiac output of up to 60% and severe hypotension.

Confirmation of haemostasis and abdominal closure

Haemostasis may be consolidated with the use of argon beam coagulation and fibrin glues.

Preoperative assessment

Preoperative assessment should be adapted to the needs of each individual patient, based on general co-morbidities and hepatic function. Patients without parenchymal liver disease are assessed as for any major intra-abdominal operation. However, patients with hepatic disease are at significantly increased risk of multi-organ dysfunction, including cardiac failure, impaired gas exchange, bleeding and renal failure so justify more detailed assessment. This may include pulmonary function testing, arterial blood gas analysis, and echocardiography. Significant numbers of patients presenting for resection of hepatic metastases will have received neo-adjuvant chemotherapy, which may reduce functional cardiac reserve. Of particular concern are conditions causing an elevation of right-side cardiac and central venous pressure (CVP) that significantly increases the risk of intra-operative bleeding. Early communication with the surgical team will identify cases with a high risk of intra-operative bleeding, large resection, or postoperative liver failure.

Patients with hepatic carcinoid present a particular challenge but the safety of these resections has been greatly improved with the use of octreotide. A full discussion of this subject is beyond the scope of this article.

Assessment of liver function

Conventional surgical teaching suggests that, in young patients (<40 yr) with normal hepatic parenchyma, it is safe to remove up to four liver segments amounting to a 50–60% resection, although survival after 80% resection is possible. However, occasionally patients develop significant postoperative liver failure after apparently safe resections, especially in those who drink significant amounts of alcohol. At present, there is no single test that will reliably predict postoperative liver failure, and the assessment is made based on laboratory and radiological investigations, quantitative tests, and surgical judgement.

The majority of patients presenting for hepatic resection surgery in the UK have normal liver parenchyma. However, primary liver tumours and cirrhosis are more common in areas of the world where viral hepatitis is endemic. Those patients with underlying chronic liver disease presenting for liver resection are at high risk of postoperative liver failure and merit more detailed assessment of hepatic function.

The Child-Pugh clinical scoring system (Table 1) has been used as a reliable, validated prognostic tool for patients with chronic liver disease undergoing general or porto-caval shunt surgery and has gained widespread use in hepato-biliary surgery. It has recently been suggested that patients with scores of B or C should not receive liver resection surgery. Any elevation of bilirubin or prothrombin time (PT) should prompt a search for a remediable cause, such as obstruction of the biliary tree. Risk stratification can be further improved with specialized testing of hepatic function, most commonly an assessment of indocyanine green (ICG) retention.
Anaesthesia for hepatic resection surgery

Table 1 The Child-Pugh scoring system. Child-Pugh total score A, 5–6 points; B, 7–9 points; C, 10–15 points

<table>
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<th>2</th>
<th>3</th>
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<td>Ascites</td>
<td>None</td>
<td>Small or diuretic controlled</td>
<td>Tense</td>
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<tr>
<td>Encephalopathy</td>
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<td>Mild</td>
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that measures liver perfusion and biliary excretion. ICG is a dye that binds to albumin and is actively taken up into liver parenchymal cells and excreted into the bile. The plasma clearance of ICG can be measured by plasma sampling or non-invasive spectrophotometry. Impaired clearance of ICG is suggested when more than 15% of the dose remains in the plasma 15 min after injection.

**Perioperative management**

**Monitoring**

AAGBI minimum standards of monitoring are applied. Sudden, catastrophic bleeding is possible. Large bore intra-venous access must be established and a rapid infusion system should be immediately available. In addition, invasive arterial and CVP monitoring allows for better haemodynamic control and regular blood sampling. Patients with cardiac disease may benefit from cardiac output monitoring, enabling greater stability during the cardiovascular changes associated with vascular occlusion. Trans-oesophageal echocardiography, pulmonary artery catheterization and arterial waveform based techniques have all been described. Hypoglycaemia is a real concern especially during hepatic vascular occlusion and after specimen resection, so blood glucose should closely be monitored. Naso-gastric and naso-jejunal tubes are inserted to enable postoperative stomach drainage and enteral feeding. Hypothermia can cause vaso-constriction and coagulopathy. Core temperature should be monitored and normothermia maintained using warmed fluids and forced warm air blankets. Intra-operative coagulation profile should be monitored and corrected with fresh frozen plasma, or as indicated from laboratory results. Neuromuscular block should be monitored.

**Conduct of anaesthesia**

The procedure is performed under standard general anaesthesia involving tracheal intubation and controlled ventilation. There is little evidence to favour any particular choice of anaesthetic agent, although hepatic clearance will be reduced after resection. Nitrous oxide should be avoided as it causes gut distension and there is a small risk of air embolism. Clearly, known hepatotoxins such as halothane should not be administered. Antibiotic prophylaxis of cefuroxime and metronidazole is given routinely, although local policy may suggest suitable alternatives.

**Analgesia**

It has been argued that the measurable short-term post-resection impairment of coagulation could increase the risk of epidual haematoma, and some authors have advocated avoidance of epidual catheters or use only in highly selected patients. However, evidence of increased adverse incidents is lacking and epidual analgesia has become established in liver resection surgery, although the coagulation abnormalities require extra care in patient selection. After operation, transfusion of fresh frozen plasma may be necessary to cover epidual catheter removal in patients with prolonged prothrombin time. Opioid i.v. patient-controlled analgesia systems and single-shot neuraxial opioids are alternatives to continuous epidual analgesia.

**Strategies to reduce intra-operative bleeding**

Blood loss of >10 litre has been reported after liver resection, and large transfusions are a risk factor for major postoperative complications and liver failure. Patients with cirrhosis, steatosis, and after chemotherapy are at especially increased risk of coagulopathy and bleeding. However, modern, multi-modal perioperative techniques have reduced mean blood loss to 300–900 ml. The use of intra-operative cell salvage in surgery for malignancy remains controversial.

The features of the coagulopathy seen in hepatic disease include reduced synthesis of coagulation factors and inhibitors, quantitative and qualitative platelet defects and hyperfibrinolysis. Coagulopathy may be induced or exacerbated by acidosis, hypothermia, and hypocalcaemia, all of which should be monitored and treated.

**Low CVP**

During parenchymal resection hepatic inflow occlusion, the main source of bleeding is backflow from the valveless hepatic veins. The control of central and thus hepatic venous pressure is crucial to reduce the blood loss. It has been well documented that a CVP of >5 cm H\(_2\)O significantly increases bleeding. However, the risks of maintaining a low CVP include cardiovascular instability and air embolism, but the theoretical risk of increasing postoperative renal dysfunction does not appear to be clinically important. Some patients require a CVP of >5 mm Hg for cardiovascular stability, and in these patients an individually tailored compromise needs to be achieved. Most patients will become hypotensive after induction, especially if an epidural is used, which can initially be treated with head down tilt and infusions of vasoconstrictors such as phenylephrine or an inotrope such as low-dose dobutamine (<3 μg kg\(^{-1}\) min\(^{-1}\)). Pre-resection fluid transfusion should be restricted although small colloid boluses may be appropriate if urine output falls to <0.5 ml kg\(^{-1}\) h\(^{-1}\) or in the presence of refractory hypotension. High CVP can be treated with diuretics or nitrate infusion. After the resection phase, circulating blood volume can be restored as the risk of bleeding, while still present, is much reduced.
Surgical access to posterior liver tumours may involve transient compression of the inferior vena cava, which can cause profound hypotension. Fluid transfusion will maintain blood pressure during these episodes but will also elevate CVP and promote bleeding. The best management of this situation involves cautious fluid transfusion and close communication with the surgical team. Positive end expiratory pressure not only reduces lung atelectasis but also elevates CVP and reduces liver blood flow, so should be avoided during the resection process.

**Aprotinin**

Significant reductions in blood transfusion requirements have been shown in liver resection using aprotinin although serious safety concerns have been raised about the incidence of life threatening allergic reactions, thrombotic potential, and renal failure. Lentschener et al. cautioned against the routine use of aprotinin in liver transplantation, although a recent Cochrane review did not confirm this. However, after the BART study, the license for aprotinin has effectively been withdrawn because of a 1.5 times increase in mortality compared with tranexamic acid and aminocaproic acid and an inability to identify specific patients who might benefit from the drug.

**Tranexamic acid**

Blood requirements have been shown to be reduced by tranexamic acid in liver transplant and liver resection surgery. Safety concerns have not been proved.

**Strategies to reduce the incidence of postoperative liver failure**

Patients developing postoperative liver failure usually start to show symptoms and signs around 72 h after surgery, developing jaundice, encephalopathy, and coagulopathy. Overall, postoperative hepatic insufficiency occurs around 3% of cases and remains a leading cause of mortality in these patients. However, the majority of cases are in patients with pre-existing cirrhosis or biliary tract obstruction, which have a reported incidence of fatal liver failure up to 32%. The aetiology of postoperative liver failure is usually multi-factorial but includes low-volume liver remnant, hepatic ischaemia, and blood loss, so the incidence may be reduced with careful surgical and anaesthetic techniques.

**Ischaemia–reperfusion injury**

Blood loss has conclusively been shown to be reduced when hepatic inflow occlusion is used. However, the inevitable warm ischaemia and subsequent reperfusion injury contribute to post-operative hepatic dysfunction. Indeed, sinusoidal endothelial cells may survive a period of ischaemia but die on reperfusion. Microcirculatory changes associated with reperfusion reduce sinusoidal blood flow and prolong any hypoxic insult.

Ischaemic pre-conditioning (a short period of ischaemia followed by reperfusion before prolonged ischaemia during the surgical procedure) and an intermittent clamping technique (10–15 min ischaemia followed by 5 min of reperfusion) have both been shown to provide effective protection from hepatic injury, although the exact cellular mechanisms are unclear. Continuous warm ischaemia times of up to 60 min and intermittent total ischaemia time of up to 90 min appear well tolerated in non-cirrhotic livers.

Endogenous anti-oxidants undoubtedly limit the damage caused by oxygen-derived free radicals, but are degraded after reperfusion. The administration of exogenous antioxidants has been shown to modify hepatic ischaemia–reperfusion injury in liver transplantation. N-acetylcysteine is routinely administered in some centres as an infusion, from induction of anaesthesia until hepatic function recovers, although evidence of clinical benefit is equivocal.

**Postoperative management**

Up to 30% of liver resection patients will have a significant complication, especially major bleeding, liver or renal dysfunction, respiratory failure, systemic sepsis, and intra-abdominal infection. Risk factors for complications include ASA grading, age, extent of liver resection, need for blood transfusion, and pre-existing cirrhosis.

**Normal postoperative course**

The enhanced blood supply to the regenerating liver remnant is associated with increased splanchnic blood flow and cardiac output. At the same time, 50% of patients will also develop self-limiting ascites during the first 48 h, which can cause hypovolaemia. A transient early increase in serum hepatic transaminase and alkaline phosphatase levels as a result of hepatocellular damage is common, but a persisting elevation suggests ongoing hepatic ischaemia. A low serum urea on the first postoperative day is an early sign of liver dysfunction.

**Postoperative care**

Most patients can be extubated at the end of surgery and are nursed in a critical care ward. Patients at low risk of hepatic dysfunction (resection of <50% in non-cirrhotic livers) can be managed as any other major laparotomy, with particular attention to prevention of hypovolaemia because of ascites. Paracetamol should not be given until liver function has returned to normal. Early postoperative enteral nutrition is likely to maintain gut function and immunocompetence. Electrolyte abnormalities including hypo-phosphataemia are common.

Patients at high risk of postoperative hepatic dysfunction justify more specialized management. Some units institute protocol-based...
care designed to maintain normal physiological parameters in patients with hepatic dysfunction and prevent progression to liver failure.

Hypoglycaemia as a result of impaired hepatic mobilization of glucose is a concern in high-risk patients or large resections and may necessitate glucose infusion. Secondary hyperaldosteronism is also common and promotes sodium and water retention and oedema, which is prevented by restriction of sodium intake and treated with diuretics. However, excessive sodium restriction or dextrose administration can cause hyponatraemia. Intra-vascular volume expansion is best performed with 20% albumin solution. The exact balance of fluid transfusion will be determined by the size of resection, plasma electrolytes and glucose measurements, and volaemic status of the patient.

Further protocol therapy consists of peptic ulcer prophylaxis with a proton pump inhibitor, regular nasogastric (NG) lactulose to prevent gut stasis that contributes to encephalopathy, continuation of N-acetylcysteine infusion and correction of electrolyte and coagulation abnormalities.

Postoperative drowsiness and confusion are commonly caused by neuraxial or systemic opioid administration, which responds to simple changes in administration. However, these patients should be carefully assessed for more serious pathology. Hypoglycaemia is treated with further dextrose infusion. Encephalopathy must be considered in a patient with deteriorating liver function and unexplained neurological symptoms. Measurement of blood ammonia may be useful if the diagnosis is unclear. Encephalopathy is treated with cardio-respiratory optimization, further lactulose and may require invasive ventilation. The molecular adsorbents recirculating system has been described as short-term support during regeneration for patients developing liver failure after resection.

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References


Please see multiple choice questions 1–3