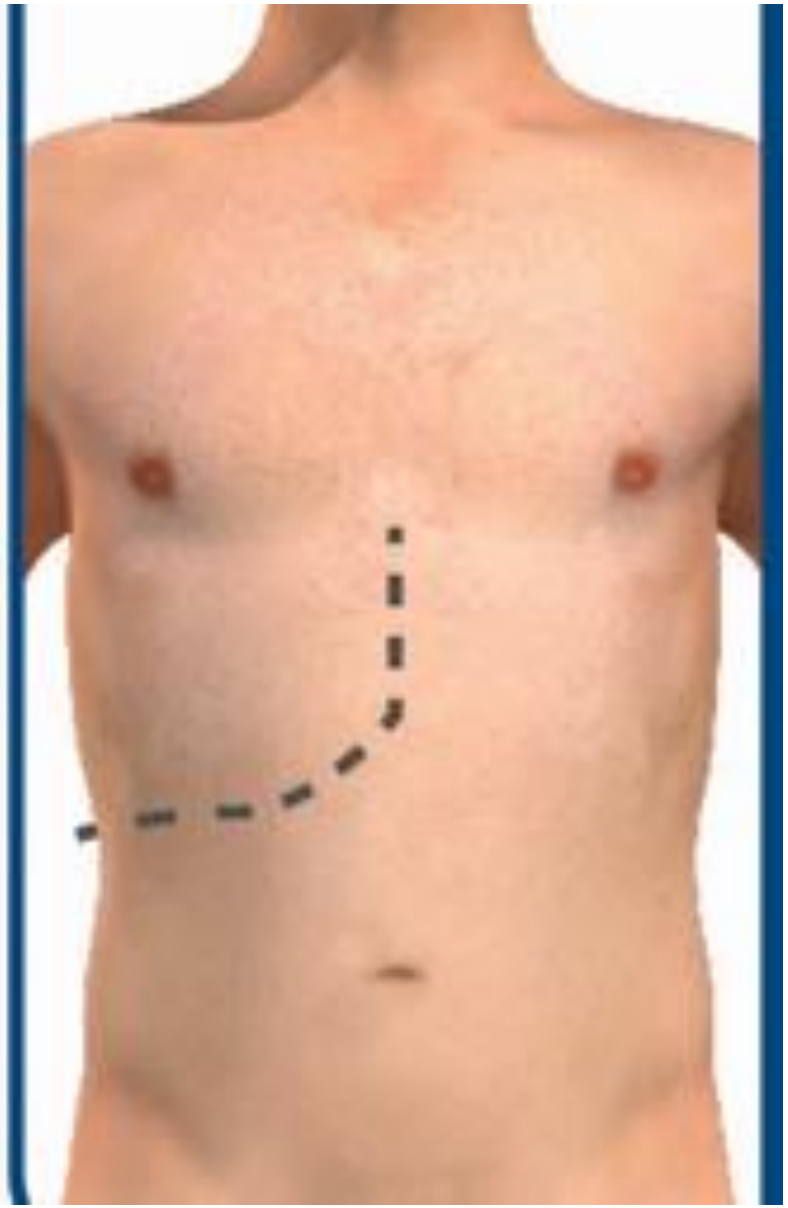
Liver Tumours

Prof. AMNA JAVED

Surgical Unit-2

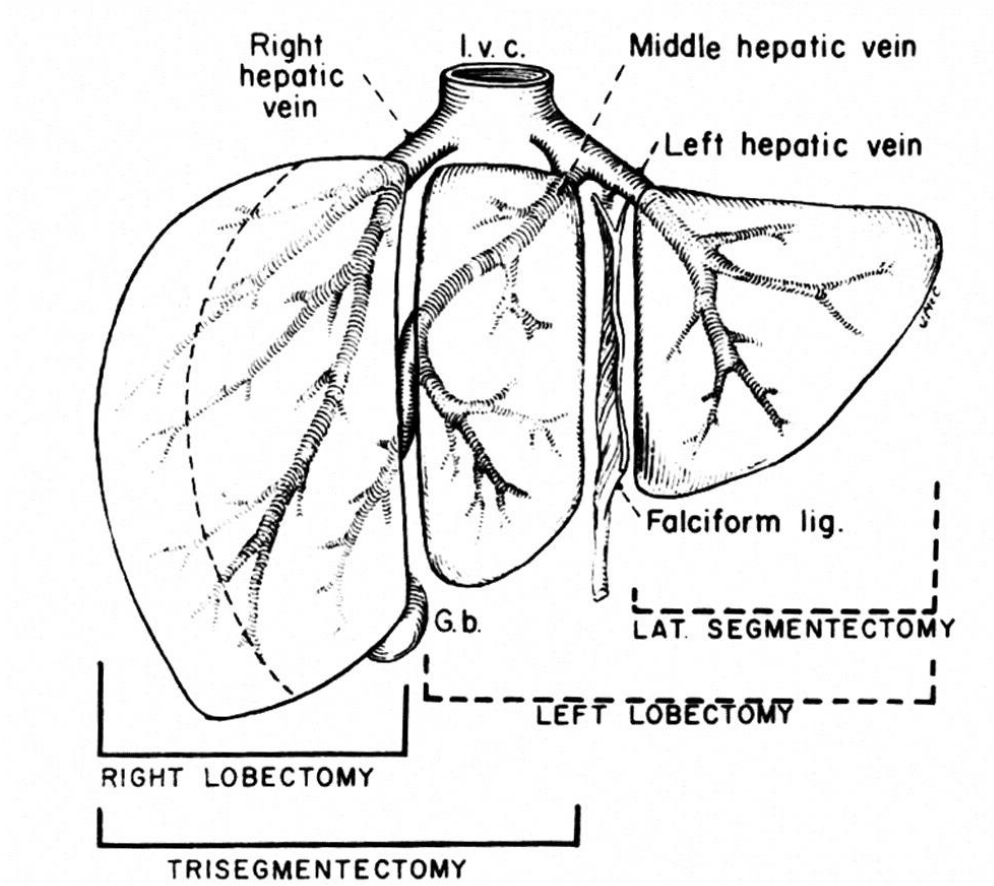
Surgical approaches to resection of liver tumours

- Adequate exposure of the liver is a prerequisite
- A transverse abdominal incision in the right upper quadrant with a vertical midline extension to the xiphoid provides excellent exposure.
- Incision can be extended across the midline transversely in the left upper quadrant if needed
- Thoracoabdominal incisions are very rarely required.



Mobilization of the liver

- The **falciform ligament** is first divided and followed along the anterosuperior surface of the liver towards the suprahepatic IVC.
- The **left triangular ligament** is divided, facilitated by placing a swab in front of the oesophagogastric junction.
- The **right triangular ligament** is then divided by retraction of the diaphragm away from the right lobe.
- On exposure of the **bare area of the liver**, the IVC can be seen as it passes behind the liver, and this can be slung above the renal veins below the liver and at the level of the main hepatic veins.
- Mobilisation of the liver is completed by division of the **lesser omentum**.
- Separating the liver from the IVC is achieved by lifting the liver anteriorly, to expose the multiple small veins (inferior hepatic veins) passing between the liver parenchyma and the IVC. These should be suture ligated to ensure haemostasis


Right hepatic vein
I.v.c.
Middle hepatic vein
Left hepatic vein
Falciform lig.
G.b.
LAT. SEGMENTECTOMY
LEFT LOBECTOMY
RIGHT LOBECTOMY
TRISEGMENTECTOMY

Dissection of the hilum

- The peritoneum overlying the hilum is divided.
- The CBD is then exposed on the free edge of the lesser omentum, mobilization being facilitated by ligation and division of the cystic duct and artery followed by removal of the gallbladder.
- Slinging the CBD with an elastic sling allows exposure of the common hepatic artery and dissection of the main right and left branches. These again may be slung to allow the remaining lymphatic tissue surrounding the portal vein to be ligated and divided.

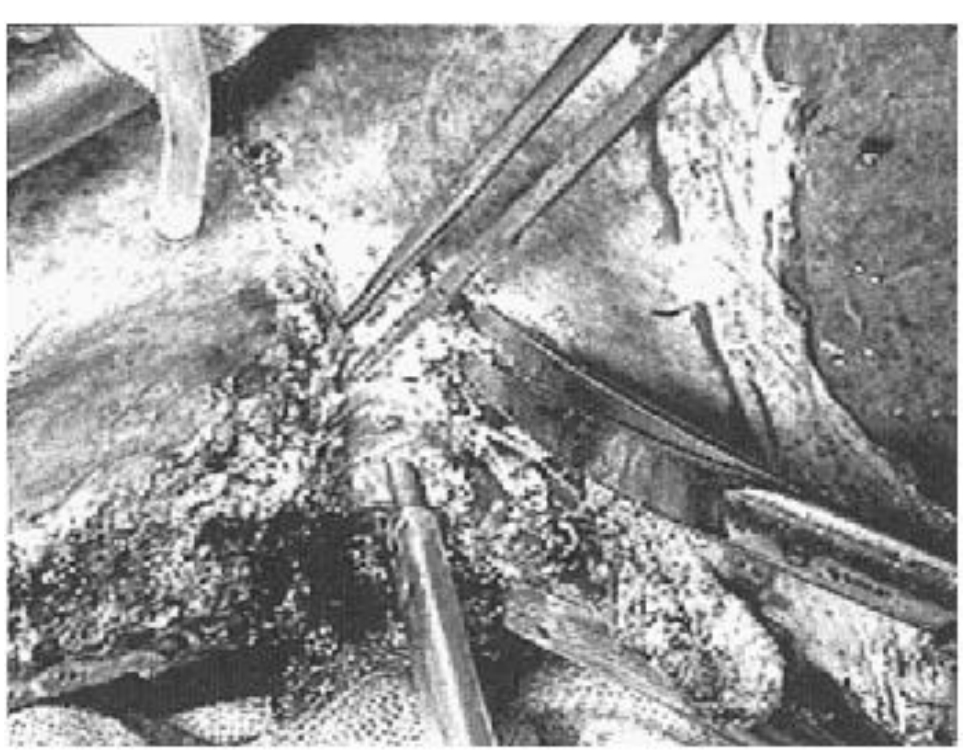
Dissection of the hilum

- The possibility of a replaced right hepatic artery should be sought arising from the superior mesenteric artery and lying posterior to the bile duct (25% of people), and an accessory left hepatic artery from the left gastric artery in the lesser omentum (25% of people).
- Dissection of the hilar bile ducts requires careful retraction on segment IV of the liver, and division of the small vessels and bile duct branches passing between segment IV and the confluence of the right and left hepatic ducts.

Division of the parenchyma: hemihepatectomy

- Once the liver has been adequately mobilized and the hilar vessels have been exposed, the main inflow vessels and bile duct to the liver to be resected can be divided.
- The arterial branch, bile duct and portal vein branch are all suture ligated. For a hemihepatectomy, division of the inflow vessels in the portal pedicle produces a line of demarcation between the right and left liver, passing to the right of, and parallel with, the falciform ligament. The parenchyma is divided along this plane of demarcation, commencing by diathermy of the liver capsule.
- As the parenchyma is divided, vessels and bile duct branches are diathermised or ligated depending on their size.
- Dissection continues on until the hepatic vein branches are approached from within the liver parenchyma, when they are ligated or stapled then divided. Alternatively, the hepatic veins can be divided outside the liver at the time of mobilisation (Figure 65.20).

- The ultrasound dissector **(CUSA®, Cavitron ultrasonic surgical aspirator)** is the most common method used for division of the parenchyma, but alternative methods including stapling, Kelly-clasia crushing and Aquaseal have all been used. Prospective evidence suggests there is no difference in speed of transection or blood loss between these methods.



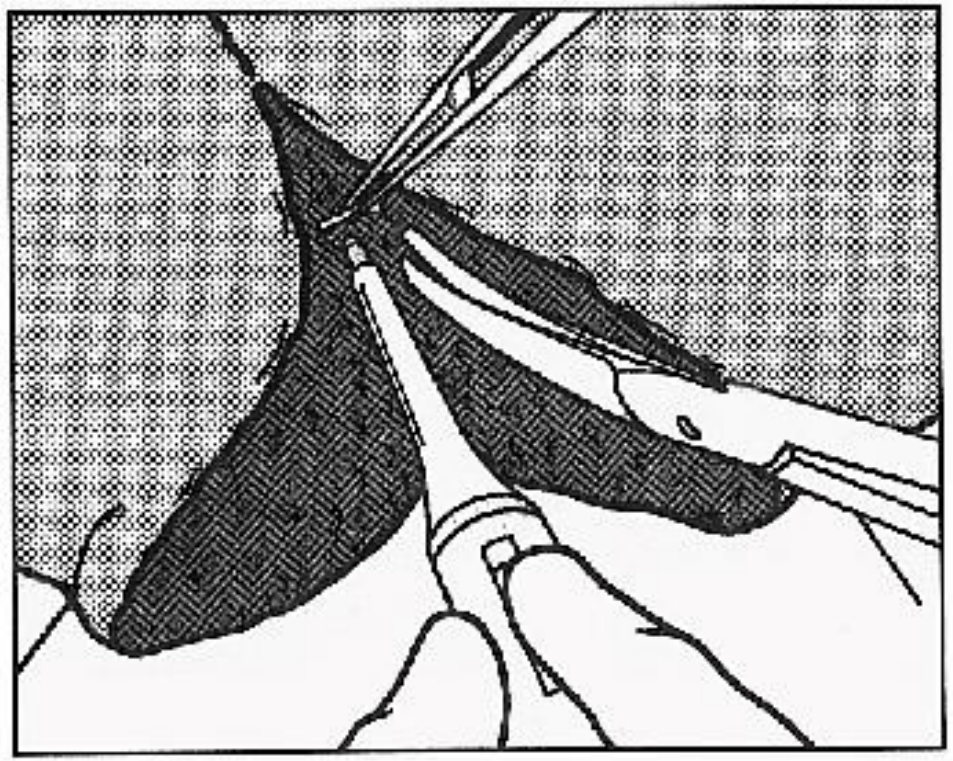


Fig. 2. Hepatic parenchymal resection by the Cavitron Ultrasonic Surgi-

Segmental and local resections

- Traditional removal of the entire liver segment or hemiliver containing disease, provides largest possible negative margin.
- **Anatomical resection** remains the treatment of choice for patients with HCC
- In case of liver metastasis a **parenchymal-sparing non-anatomical approach** involving multiple metastectomies is now considered the standard of care. This approach has,
  - No impact on long-term oncological outcome
  - Preserves liver remnants
  - Allows further resection in the case of recurrent disease

Figure 65.20 Hepatectomy post resection. Cut surface of the residual liver following a right hepatectomy in which segments V–VIII have been removed. On the lower edge, the portal vein and bile duct can be visualised.

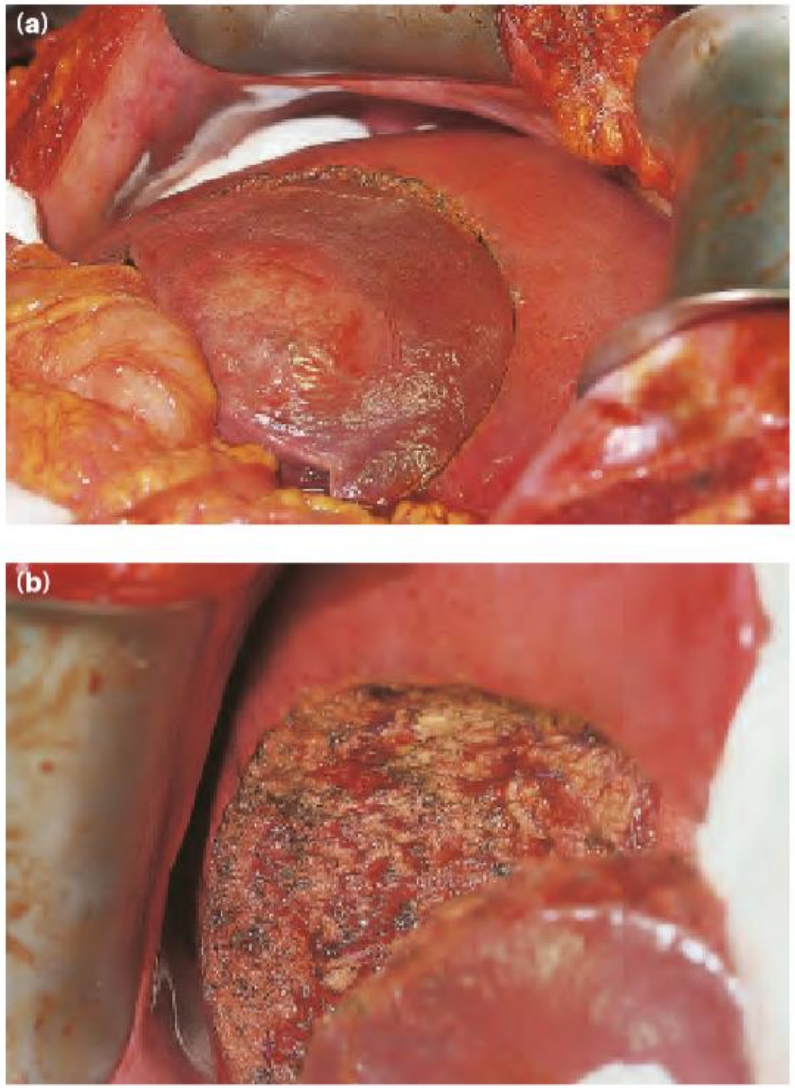
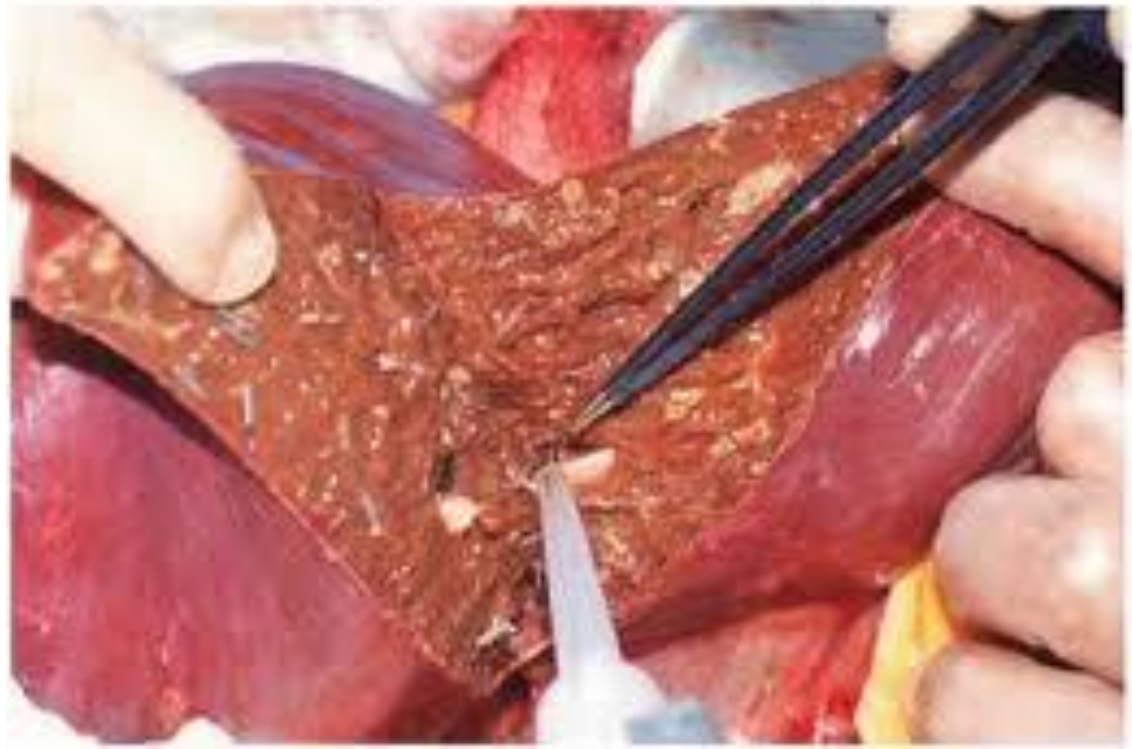


Figure 65.21 (a, b) Segmental resection. Removal of a primary liver tumour by resection of liver segment VI in a patient with well-compensated liver cirrhosis.

CT scan of colorectal liver metastases initially deemed unresectable before (a) and after chemotherapy (b), by which time these tumours are easily resectable.



Laparoscopic liver resections

- Laparoscopic liver surgery aims to provide curative resection while minimising blood loss and postoperative time to recovery.

Blood loss and transfusion

- Resection is often possible without blood transfusion.
- Minimal blood loss during liver resection can be made possible by,
  - Better understanding of the segmental anatomy of the liver
  - Better patient selection for surgery
  - Low central venous pressure anaesthesia (<10 mmHg)
  - Better control of the coagulation cascade – can be achieved using TEG
  - The antifibrinolytic drug aprotinin has significantly reduced bleeding in patients with liver disease and an underlying coagulopathy.
  - Oozing from the resected surface of the remnant liver can be reduced by the topical application of fibrin glue or fibrin-impregnated collagen fleece.
  - The main alternative is use of an argon-beam coagulator.
  - Intermittant temporary clamping of the portal vein and hepatic artery in the hepatoduodenal ligament (**Pringle manoeuvre**) can reduce blood loss during parenchymal transection. The optimal duration of the Pringle manoeuvre is unknown, but it can be applied intermittently, e.g. cycles of 15 minutes inflow occlusion followed by 5 minutes of reperfusion, until parenchymal transection is complete.

Ablation for liver tumours

- Ablative therapies aim to destroy tumour by the direct application of energy to discrete lesions. It can be performed percutaneously, laparoscopically or at open surgery.
- Patients with small volume resectable lesions who are not sufficiently fit to undergo liver resection should be considered for ablation, as should those with limited liver metastases who have insufficient liver volume to undergo resection.
- A **combined resection/ ablation approach** has also been advocated.

Ablation for liver tumours

- **Radiofrequency ablation (RFA)** is the most widely used ablative technique and relies on direct current transmission through tissue to generate heat and ablation of the tumour.
- Increasing lesion size leads to exponential increases in resistance to current, limiting the size of the effective ablation zone and explaining the increased risk of local recurrence and diminished survival with lesions >3 cm.
- **Microwave ablation** has been designed to overcome some of the limitations of RFA and offers higher intratumoural temperatures, larger tumour ablation volumes and faster ablation times. Despite this, local recurrence after microwave ablation has been reported at between 5% and 13%.

Benign liver tumours

- Haemangiomas:
  - These are the most common liver lesions.
  - They consist of an abnormal plexus of vessels, and their nature is usually apparent on ultrasound.
  - In case of diagnostic uncertainty, CT scanning with delayed contrast enhancement shows the characteristic appearance of slow contrast enhancement due to small vessel uptake in the haemangioma.
  - Usually multiple in number.
  - Lesions found incidentally require radiological confirmation of their nature and no further treatment.
  - Giant hemangiomas can rupture therefore resection for large lesions should be considered, especially if they appear to be symptomatic.
  - Diagnosis is usually incidental, and surgical resection only recommended if patients are significantly symptomatic or significant diagnostic uncertainty remains after multimodal imaging.

- Hepatic adenoma:
  - Adenomas are benign liver tumours seen almost exclusively in women aged between 25 and 50 years.
  - These well-defined and vascular lesions are classically associated with use of the **oral contraceptive pill**, and are generally solitary.
  - The majority are found incidentally on imaging, although up to one-third may present with pain because of rupture or bleeding.
  - There is malignant potential, with up to 10% developing into hepatocellular carcinoma.
  - The risk of rupture and malignancy means that surgical excision is generally recommended if >5 cm in size, although some lesions may regress after discontinuation of the oral contraceptive pill.

- Focal nodular hyperplasia:
  - Unusual but not uncommon. Aetiology is unknown
  - There is a focal overgrowth of functioning liver tissue supported by fibrous stroma.
  - Patients are usually middle-aged females, and there is no association with underlying liver disease.
  - Ultrasound shows a solid tumour mass.
  - Contrast CT or MRI may show central scarring and a hypervascular lesion.
  - FNH contains both **hepatocytes** and **Kupffer cells**. MRI using liver-specific contrast agents, such as gadoxetic acid, which is taken up by hepatocytes and excreted in bile, or superparamagnetic iron oxide, which is taken up by Kupffer cells, may be useful in determining the hepatocellular origin of FNH and allowing differentiation of FNH from metastatic cancer.
  - FNH does not have any malignant potential and once the diagnosis is confirmed, does not require any treatment or follow-up.

Colorectal liver metastases

- Around 30% of patients with colorectal cancer will have metastatic disease at the time of presentation, and a further 20% will develop liver disease after the primary colorectal malignancy has been resected.

Defining resectability for colorectal liver metastases

- Resectability with curative intent is defined as the ability to successfully remove all residual disease from the liver with clear surgical margins, while leaving adequate disease-free viable liver tissue to sustain life.
- Technical contraindications to resection are related to the anatomical location of metastases, mainly due to close proximity to major vascular or biliary drainage structures.
- The boundaries of technical resectability have been extended by the development of techniques such as total vascular exclusion, which offer hope for certain patients with involvement of major vessels.
- Resection with a negative surgical margin of 1 cm (R0) has always been considered the gold standard, but in an era of effective modern chemotherapy, patients with R1 (microscopically negative) resection have similar survival to those with R0 resections.

Defining resectability for colorectal liver metastases

- A future liver remnant (FLR) of 25% preoperative volume is considered sufficient to prevent postoperative hepatic failure, although patients with impaired hepatic function, including those with chemotherapy-induced liver damage, may require a larger FLR.
- The regenerative nature of liver parenchyma means that significant regrowth takes place after resection, and this unique feature means that two-stage procedures are feasible, with parenchymal regeneration between resections ensuring adequate FLR.
- This regenerative capacity can be further manipulated further using preoperative portal vein embolisation (PVE) to cause reactive hypertrophy in the proposed FLR.
- The ALPPS procedure (associating liver partition and portal vein ligation for staged hepatectomy) combines both these procedures, maximizing hypertrophy of the FLR, but is associated with significant operative mortality (10%) and morbidity (>50%).

Defining resectability for colorectal liver metastases

- For some patients, a combination of resection and thermal ablation may also offer long-term benefits.
- Oncological contraindications to hepatic resection include unresectable extrahepatic malignancy.
- Long-term survival is now possible in selected groups of patients with resected extrahepatic disease.
- Survival after lung resection for colorectal metastases is similar to that seen after liver resection, with most series quoting a 5-year survival in the order of 40–50%, with low operative morbidity and mortality.

Staging and selection of patients for liver surgery

- Patients with colorectal liver metastases must be fully staged prior to any treatment plan and this should be coordinated by a specialist multidisciplinary team.
- Routine staging commonly involves
  - Triple phase CT chest/abdomen/pelvis
  - Contrast MRI scan of the liver
  - Whole body PET-CT to identify metastatic disease.

Chemotherapy for colorectal liver metastases

- Majority of patients with colorectal liver metastases should receive perioperative chemotherapy irrespective of their initial resectability, with the rationale that this will result in the destruction of occult disease, where progression despite chemotherapy signifies poorer prognosis, as well as reducing lesion size and so improving resectability.
- A subgroup of patients having non-resectable lesion at presentation, but become resectable after systemic chemotherapy as lesions decrease in size and move away from critical vascular and biliary structures.
- Chemotherapy with 5-fluorouracil (5FU) and folinic acid produces a response rate of approximately 30% but, when combined with oxaliplatin, the response rate increases to 50–60%, often with a dramatic size reduction of the lesions.
- The combination of chemotherapy with monoclonal antibodies (mAbs) that recognise vascular endothelial growth factor receptor (VEGFR) or the epidermal growth factor receptor (EGFR) may provide additional benefit.

Figure 65.23 Colorectal liver metastases on a computed tomography scan.

Hepatocellular carcinoma

- HCC comprises the overwhelming majority of primary liver cancers, with a steadily rising global burden. There is wide variation in the geographical incidence of HCC
- HBV as a risk factor for HCC. HBV vaccination programmes have led to falls in the incidence of HCC.
- Hepatitis C virus (HCV) increases the risk of HCC by 17 times, primarily by promoting end-stage liver disease.
- Lifetime alcohol exposure correlates with the incidence of HCC. Hepatic metabolism of alcohol is thought to lead to the production of free radicals, causing intracellular oxidative stress eventually leading to a chronic inflammatory state.
- Because of the critical role of the liver in glucose metabolism, obesity and diabetes mellitus (both of which involve impaired glucose handling) are significant independent risk factors for the development of HCC, and the global rise in obesity and diabetes is likely to lead to a significant increase in HCC developing on a background of hepatic non-alcoholic fatty liver disease (NAFLD).
- Cohort studies have suggested that 60% of patients with HCC die of cancer-related causes, with the remaining 40% succumbing to underlying parenchymal liver disease. It is therefore critical that treatments for patients with HCC are considered in the context of both the cancer and the underlying parenchymal disease.

Staging of hepatocellular carcinoma

- Most commonly used Clinical staging systems for HCC is the Barcelona Clinic Liver Group (BCLC) staging system, which was initially designed to define both prognosis and optimal treatment for patients with HCC.
- Underlying liver function is assessed using the CTP system

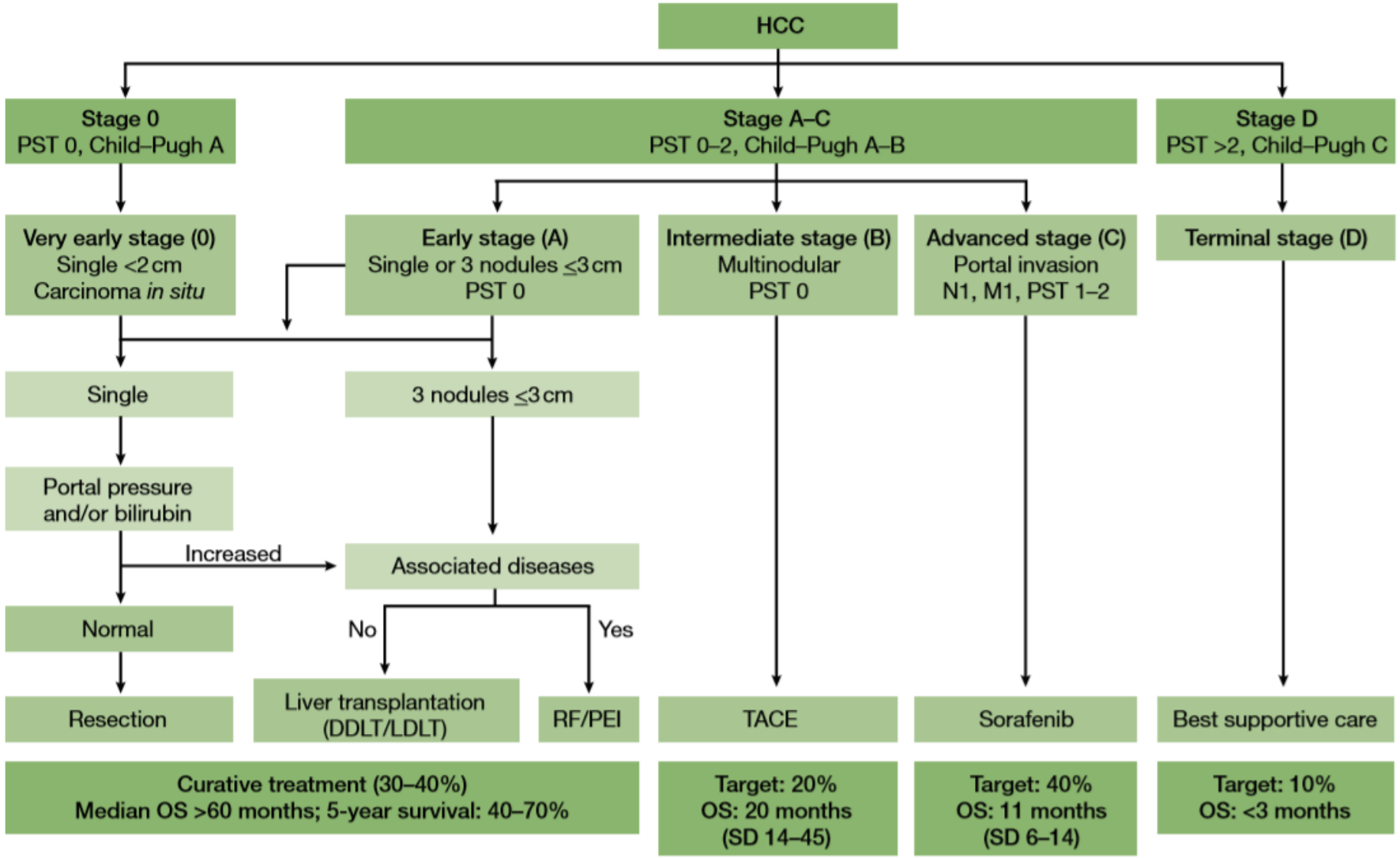


Figure 65.24 The Barcelona Clinic Liver Group staging system for the management of hepatocellular carcinoma (HCC). Patients with asymptomatic early tumours (stage 0–A) are candidates for curative therapies (resection, transplantation or local ablation). Asymptomatic patients with multinodular HCC (stage B) are suitable for chemoembolisation (TACE), whereas patients with advanced symptomatic tumours and/or an invasive tumoural pattern (stage C) are candidates for sorafenib. End-stage disease (stage D) includes patients with grim prognosis who should be treated by best supportive care. DDLT, deceased donor liver transplantation; LDLT, living donor liver transplantation; OS, overall survival; PEI, percutaneous ethanol injection; PST, ECOG performance status; RF, radiofrequency ablation; SD, standard deviation; TACE, transcatheter arterial chemoembolisation. (Reproduced with permission from Villanueva A. Medical therapies for hepatocellular carcinoma: a critical view of the evidence. *Nature Rev Gastroenterolol Hepatol* 2013; **10**: 34–42).

Surgical resection for HCC

- Only 20–40% of patients with HCC are considered candidates for surgical resection.
- However, with the introduction of surveillance programmes for those patients identified to be at risk, improved imaging and better perioperative management, surgical resection is increasingly considered the mainstay of treatment for patients with preserved hepatic function.
- Although tumour size, vascular invasion and multifocal disease are recognised as poor prognostic indicators, none is considered an absolute contraindication to surgical intervention.
- Multinodular lesions represent multiple discrete lesions occurring independently against a background of procarcinogenic parenchymal damage, or may represent aggressive tumour biology with intrahepatic metastases.
- In general, oncological contraindications to resection now include:
  (1) extrahepatic metastasis
  (2) multiple and bilobar tumours
  (3) involvement of the main bile duct
  (4) presence of tumour thrombus in the main portal vein/ vena cava.

Preoperative evaluation of patients with HCC

- Ensuring good outcome for patients undergoing surgical resection for HCC relies on an accurate assessment of tumour stage, patient fitness and underlying liver function.
- This is particularly important when considering patients for larger resections, where the function of the FLR becomes critical.
- Postoperative morbidity and mortality are known to increase with a higher CTP score
  - Major liver resection is generally only considered feasible in patients with **CTP-A** disease.
  - Minor liver resection may be considered in **CTP grade B**, but remains a high-risk procedure.
  - **CTP grade C** score patients are not candidates for liver resection.
- For some patients, inadequate FLR may the only contraindication to surgical resection. For this group, preoperative radiological portal vein embolisation can be performed to induce hypertrophy in the proposed remnant liver, increasing the FLR.

Preoperative imaging for HCC

- Triple phase CT chest/abdomen/pelvis and MRI of the liver is considered standard of care in most units.
- Both MRI and CT have limited sensitivity and specificity for detection of lesions <1 cm, although this is improved with the use of liver-specific contrast agents.
- The assessment of background liver fibrosis and cirrhosis with functional imaging techniques that use hepatospecific contrast medium can be done.
- The use of FDG-PET to exclude extrahepatic involvement has been investigated, but it remains unclear whether this offers any benefit over standard CT chest/abdomen/pelvis.

Surgical principles for HCC

- The objectives of surgical resection for HCC:
  (1) Resection of all malignant and as much preneoplastic tissue as possible
  (2) Preserving enough functional hepatic parenchyma to reduce the risk of postoperative liver failure.
- HCC spreads within the liver by direct invasion of both the portal and hepatic venous systems, and anatomical resection that includes removal of the entire venous drainage of a HCC is therefore considered the optimal approach to increase the removal of occult micrometastases.
- There is a clear long-term survival advantage to anatomical versus non-anatomical resection, and this approach is now considered standard of care where underlying liver function allows.

Disease recurrence after resection

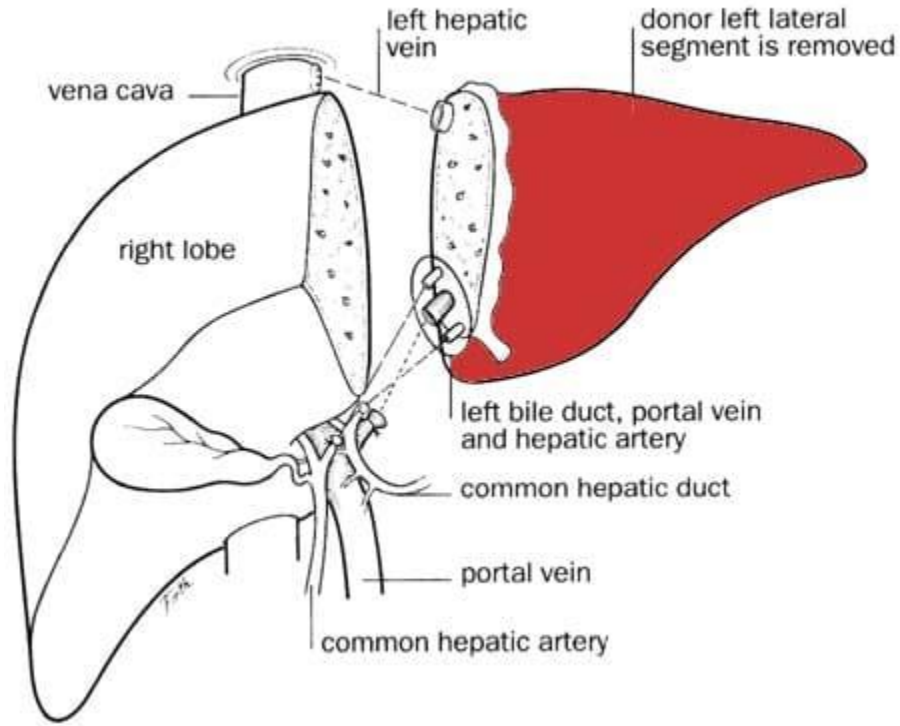
- Intrahepatic recurrence occurs in around 80% of cases within 5 years of resection.
- There are no effective neoadjuvant or adjuvant treatment options to reduce the risk of recurrence after resection.
- Intrahepatic recurrence after surgery is thought to consist of two discrete groups:
  - Patients who had missed micrometastases at initial staging
  - Patients who developed lesions de novo in diseased background liver

The most effective approach to reducing intrahepatic recurrence of HCC is to remove both of these possibilities by performing liver transplantation.

Liver transplantation

- Liver transplantation for HCC offers the advantage of not only definitively treating the tumour but also removing the diseased hepatic parenchyma, so reducing the potential for intrahepatic recurrence.
- Mazzaferro described The concept of organ transplantation for primary liver cancer in 1996, (who performed liver transplantation for patients with one hepatocellular carcinoma of ≤5 cm, or up to three nodules of ≤3 cm, and reported a 4-year overall survival of 75% and recurrence-free survival of 83%).
- Similar results have been obtained by using the inclusion criteria (**Milan criteria**) having the benchmark indications for transplantation for HCC.
- Patients outside these criteria can also be successfully downstaged using locoregional therapies (such as ablation), and following a period of observation with adequate disease control may be considered suitable candidates for transplantation.

Adult Liver Donor



Thankyou