

# Malignant liver tumours

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**Neuroendocrine/carcinoid tumours** Carcinoids are the most common NETs affecting men and women equally. The overall incidence is steadily increasing, estimated at 1.5–1.9 clinical cases per 100 000 population, although in autopsy series this reaches 650/100 000 population. Primary carcinoid tumours in the liver are rare and hepatic lesions are almost invariably metastases from small bowel or colon. Approximately 20% of small intestine carcinoids develop metastases and 30% of these patients develop carcinoid syndrome. If the primary has been resected, liver metastases can be observed unless carcinoid syndrome develops. Hepatic carcinoid disease that is resectable should be treated but this must be preceded by a thin-slice CT scan and laparoscopy with intraoperative ultrasonography if doubt remains to exclude small-volume disease. Carcinoid syndrome is a difficult clinical problem, especially when pharmacological approaches are ineffective; in these patients, debulking should be considered. Some patients will develop a small number of lesions of similar sizes that can often be resected with curative intent. A significant proportion will develop recurrence(s), but this may take 18–36 months and further surgery is often possible. When lesions are numerous and of different generations (sizes) there are no surgical options and ablative, transarterial embolisation or targeted treatment with somatostatin analogues should be considered.

**Hepatocellular carcinoma (HCC)** HCC is a malignant tumour arising from hepatocytes and is the most common primary liver cancer. There is a steadily rising global burden. In 2016 there were 1 million incident the fifth most common cause of cancer in men and the seventh - in women, representing a third of all cancer-related deaths. HCC is the leading cause of death in patients with cirrhosis, affecting three times more men than women. There is wide variation in geographical incidence. More than 80% of cases occur in Asia and sub-Saharan Africa, with an incidence of 99/100 000 compared with 5/100 000 in Europe. Geographical variation reflects the incidence of aetiological factors. Chronic hepatitis B virus (HBV) infection accounts for >50% of cases worldwide and HBV vaccination programmes reduce the incidence in high-risk areas. Hepatitis C virus (HCV) increases the risk of HCC 17-fold by promoting end-stage liver disease. Aflatoxin contamination of rice in some parts of the world is probably responsible for seasonal variations. Lifetime alcohol exposure remains an intractable risk factor and correlates with the incidence of HCC. Obesity and diabetes mellitus are additional independent risk factors. Cancer-related causes are fatal in 60% of patients and 40% die of underlying parenchymal disease. HCC is typically diagnosed at a late stage and prognosis even in developed countries is limited with median survivals following diagnosis of 6–20 months and overall survival of less than 50% at 2 years and 10% at 5 years, with worse results in developing countries.

**Clinical staging systems for HCC** Clinical staging systems for HCC are designed to guide management. The Barcelona Clinic Liver Group (BCLC) staging system, initially designed to define both prognosis and optimal treatment for patients with HCC, is the most commonly used (Figure 69.22). As patients with HCC usually have underlying liver disease that has a marked impact on prognosis, the BCLC system was designed to reflect underlying liver function and performance status together with

tumour characteristics. Underlying liver function is assessed using the - CTP system. Treatment of hepatocellular carcinoma Surgical resection for hepatocellular carcinoma - Only 20–40% of patients with HCC are candidates for surgery , but with surveillance programmes in at-risk patients, improved imaging and advances in perioperative management resection is increasingly possible. Selecting suitable patients remains controversial and although tumour size, vascular invasion and multifocal disease are poor prognostic indicators they are not absolute contraindications. Multinodular lesions may repre - sent multiple discrete lesions occurring independently against a background of procarcinogenic parenchymal damage or aggressive tumour biology with intrahepatic metastases. Oncological contraindications include extrahepatic metastasis, multiple/bilobar tumours, main bile duct involvement and tumour thrombus in the main portal vein/vena cava. Preoperative evaluation of patients with hepatocellular carcinoma Achieving good outcomes for patients undergoing surgical resection requires accurate assessment of tumour stage, comorbidities and liver function. This is particularly important when planning larger resections, where the function of the FLR becomes critical. Postoperative morbidity and mortality increase with higher CTP scores, and major liver resection is usually only possible in patients with CTP-A disease. Minor liver resection may be considered in those with CTP-B disease but remains a high-risk procedure, and CTP-C patients are not candidates for liver resection. If inadequate FLR is the only contraindication preoperative radiological PVE should be performed. Preoperative imaging for hepatocellular carcinoma Imaging is a critical part of the preoperative assessment of HCC and accurate tumour staging and anatomical assessment is essential to determine technical and oncological resectability and exclude metastatic disease. Triple-phase CT chest/ abdomen/pelvis and MRI of the liver is the standard of care, although MRI and CT have limited sensitivity and specificity for lesions <1 /uni00A0 cm (improved with liver-specific contrast agents). FDG-PET does not appear to confer any benefit over standard imaging. Surgical principles for hepatocellular carcinoma Surgical resection is a compromise requiring resection of the tumour while preserving sufficient functional parenchyma. HCC spreads within the liver by direct invasion of portal and hepatic venous systems. Anatomical resections that include removal of the entire venous drainage of a tumour, including occult micrometastases, is the optimal approach. There are clear long-term survival benefits for anatomical versus non- anatomical resections, with anatomical resection now considered the standard of care when underlying liver function allows. Improvements in patient selection and surgical technique have reduced the 30-day mortality to <5%. Disease recurrence after resection - Intrahepatic recurrence occurs in 80% of cases within 5 /uni00A0 years and neoadjuvant or adjuvant options do not reduce the risk. Intrahepatic recurrence is thought to result from missed micrometastases or the development of new lesions and the most effective approach to reducing intrahepatic recurrence is liver transplantation.

**Stage 0 PST 0, Child–Pugh A Early stage (A) Very early stage (0) Single or 3 nodules <3cm Single**

<2cm Carcinoma in situ PST 0 3  
nodules <3cm Single Portal  
pressure and/or bilirubin Increased  
Associated diseases Normal No  
Liver transplantation Resection  
RF/PEI (DDLT/LDLT) Curative  
treatment (30–40%) Median OS  
>60 months; 5-year survival:  
40–70% Figure 69.22 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 tumoral 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 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. Nat Rev Gastroenterol Hepatol 2013; 10 : 34-42.) Stage A-C Stage D PST 0-2, Child-Pugh A-B PST >2, Child-Pugh C Intermediate stage (B) Advanced stage (C) Terminal stage (D) Multinodular Portal invasion PST 0 N1, M1, PST 1-2 Yes TACE Sorafenib Best

supportive care Target: 10%  
Target: 40% Target: 20% OS: <3  
months OS: 11 months OS: 20  
months (SD 6–14) (SD 14–45)

, living donor liver transplantation; OS, overall survival;

Liver transplantation that definitively treats the tumour and underlying cirrhosis represents an attractive option, but organ shortages mandate careful selection of patients and early experience with transplantation was disappointing. Transplantation for HCC, first described by Mazzaferro in 1996 for patients with tumours  $\leq 5$  cm or up to three nodules  $\leq 3$  cm, achieved 4-year overall survivals of 75% and recurrence-free survivals of 83%. These inclusion criteria were adopted as the Milan criteria, with angioinvasion and extrahepatic involvement as additional exclusion criteria, and are now universally accepted. Liver transplantation criteria, however, continue to evolve and 'expanded' criteria remain debated. Locoregional therapies such as ablation may downstage HCC from beyond to within the Milan criteria and following a period of observation these patients may be considered as candidates for transplantation.

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