Hepatocellular carcinoma – Full Clinical Guideline

Reference no:CG-GASTRO/2015/197

90% of HCC are associated with a known underlying risk factor (majority HBV/ HCV). 1-8% per year of patients with cirrhosis will develop HCC.

Surveillance:

NICE recommend offering ultrasound (with or without AFP) every 6 months as surveillance for HCC. Surveillance should, however, only be undertaken in those patients where early detection of HCC may lead to an alteration in management (any form of therapeutic intervention). A patient with a Child Pugh score ≥ 9 points and who was not felt to be a candidate for transplantation should not have surveillance. Potentially curative interventions such as radiofrequency ablation, surgical resection and transplantation are performed under general anaesthetic. A patient with a poor performance status or co-morbidities sufficient to preclude general anaesthetic or these interventions (including harmful alcohol consumption associated with physical dependency) should not have surveillance. For these reasons it would be unusual to commence HCC surveillance in a patient > 75 years.

It is also important to keep the appropriateness of continued surveillance under review, should new co-morbidities arise. It would be unusual to continue surveillance beyond the age of 80 years.

Surveillance with 6 monthly ultrasound and serum alpha fetoprotein should be considered in the following disease groups:

1. Patients with established cirrhosis of any aetiology

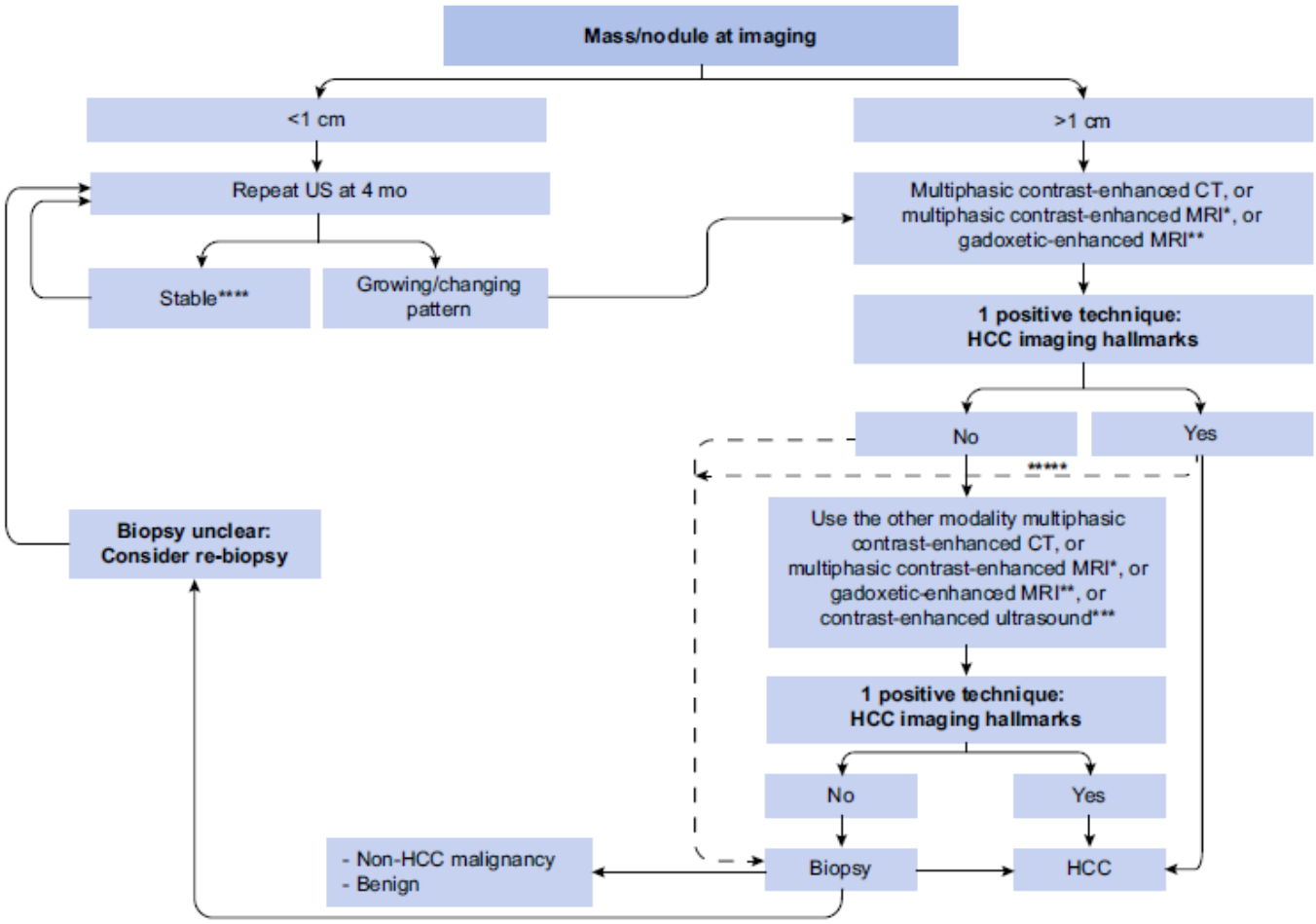
2. Patients with Hepatitis B and moderate/ severe fibrosis, not amounting to cirrhosis (Ishak stage ≥ 3) (NICE Hepatitis B 2013)

3. Consider surveillance in Hepatitis B patients with Ishak fibrosis score < 3 and > 40years and FHx of HCC and HBV DNA > 20,000IU/ml (NICE Hepatitis B 2013)

ROC analysis shows that an AFP level of 20ng/ml provides the optimal balance between sensitivity and specificity, though at this level the sensitivity is only 60%. With increasing levels the positive predictive value increases and patients with an AFP > 200ng/ml may require additional imaging if the ultrasound is normal. Patients with AFP levels 9-20ng/ml should have them repeated after 3 months.

PRACTICAL NOTE: Surveillance is coordinated by the Liver Nurse Specialists. Child Pugh Stage A patients should be followed up with annual review in the nurse led stable cirrhosis clinic, from where surveillance investigations will be arranged. The Liver Nurse specialists should be informed by letter if a patient who remains in the consultant clinic is to start a programme of surveillance. The referring doctor should request the first ultrasound and AFP. It is also the responsibility of the doctor to review these results. Forms for subsequent ultrasound and AFP will be generated automatically and the results communicated to the patient by the Nurse Specialist.

Diagnosis (assessment of a liver nodule):



- The majority of nodules < 1cm detected in a cirrhotic liver are not HCC. Nodules < 1cm in diameter detected by ultrasound should be followed with ultrasound every 4 months in the first year and with regular 6 month scans thereafter.
- The likelihood of HCC in a lesion > 2cm is high. If serum AFP > 200 ng/ml and/or one dynamic contrast enhanced scan displays typical vascular profile the positive predictive value > 95%.
- Radiologists will report the likelihood of a lesion in the liver being an HCC using the LI-RADS classification system (LI-RADS 1 – definitely benign, 2 – probably benign, 3- intermediate probability, 4- probably HCC, 5 -definitely HCC)

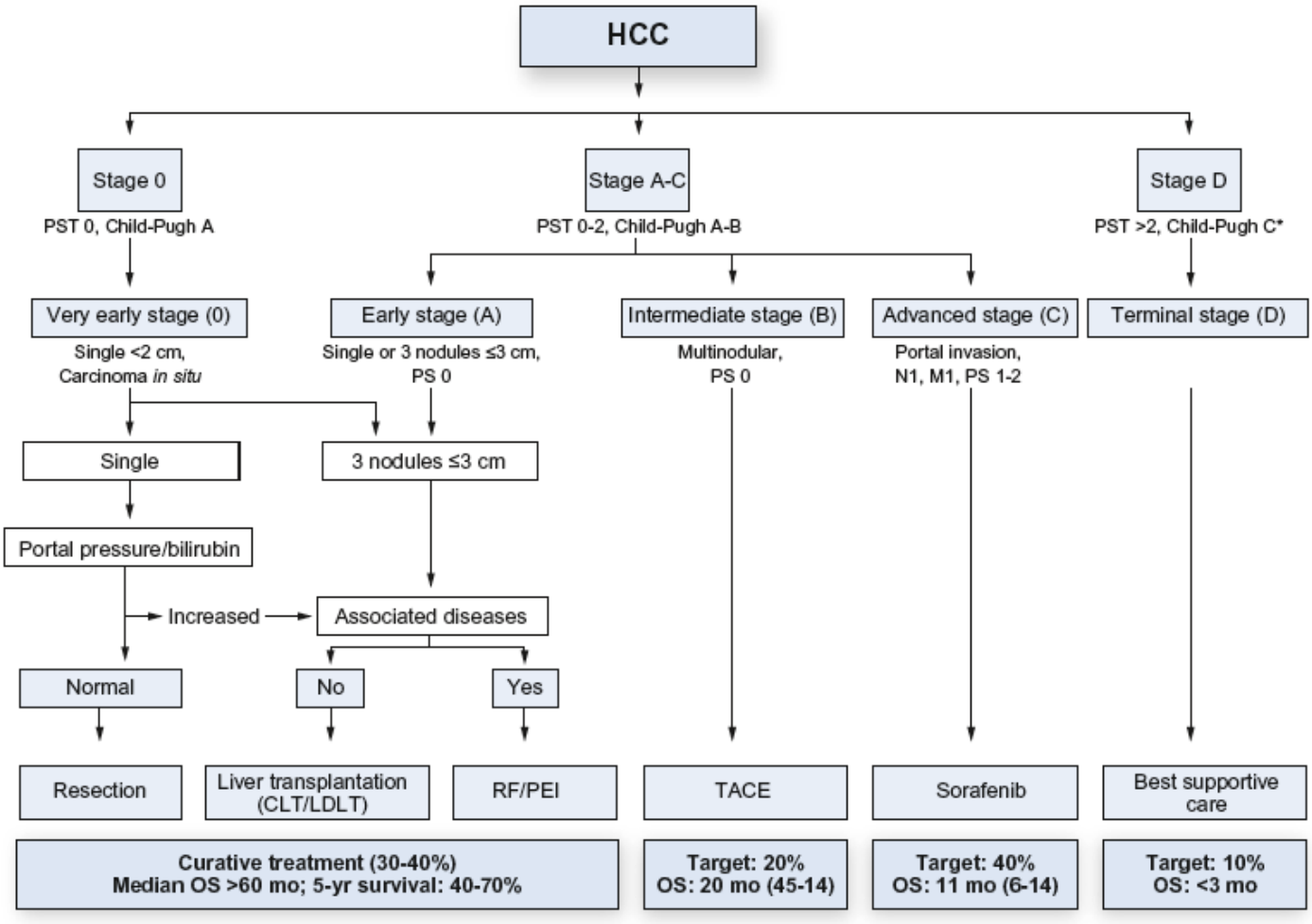
Management:

The management strategy for HCC is decided on at the HPB cancer MDT. Patients needing consideration for liver transplant should be referred to the Queen Elizabeth Hospital, Birmingham (Dr Tahir Shah or Dr Shishir Shetty). Patients in whom resection is being considered will be seen by a Consultant Hepatobiliary surgeon from Nottingham in their weekly Derby clinic. Liver resection, Trans-arterial chemoembolisation (TACE) and radio-frequency ablation are currently all performed at the Queens Medical centre, Nottingham.

- Resection is the treatment of choice in non-cirrhotic patients (5% of cases in West, 40% in Asia) or single lesions in compensated cirrhotic patients.
- Resection in cirrhotic patients requires they have a normal bilirubin and HVPG < 10mmHg (or surrogate of this – no varices/ splenomegaly and plts > 100), otherwise risk of post-operative liver failure

increases. Perioperative mortality is of the order of 2-3%. A MELD score of ≤ 8 is associated with a 0% risk of liver failure post resection.

- Liver transplantation is the treatment of choice for cirrhotic patients who fall within the Liver Advisory Group/ NHSBT modification of the Milan Criteria.
  Solitary HCC ≤ 5cm or ≤ 5 lesions all ≤ 3cm or exceptionally solitary lesions between 5 and 7cm that are stable in size over 6 months with or without locoregional therapy; AFP ≤ 1000
  No vascular invasion or extrahepatic disease on CT CAP
- TACE is recommended for HCC that are unresectable or outside of transplant criteria, without vascular invasion or extra-hepatic spread. Patients should have compensated disease (Child Pugh A or B7 without ascites), no portal vein thrombosis and eGFR > 30. ***The HAP score (see below) can help in selecting patients for TACE based on their likely outcome***
- Microwave ablation is considered for patients with up to 3 small HCC (typically ≤ 3cm) not suitable for surgery. Treatment of subcapsular, subdiaphragmatic, or lesions in close proximity to the gallbladder may not be possible due to risk of thermal injury (these lesions may be amenable to alcohol injection). Treatment of lesions in close proximity to vessels may be less effective due to heat sink.
- Systemic therapies are only indicated for patients with advanced stage tumours and well preserved liver function (Child Pugh A). Histological confirmation is required. Sorafenib (multi tyrosine kinase inhibitor) increased median survival from 7.9 to 10.7 months in the SHARP study. Atezolizumab PD-L1 checkpoint inb) + Bevacizumab (anti-VEGF) was associated with a median survival of 17.1 months in the IMbrave study. Varices must be treated first as VEGF inb associated with increased risk of bleeding.



Barcelona- Clinic liver cancer (BCLC) staging system and treatment strategy - reproduced from EASL-EORTC clinical practice guidelines on management of HCC 2012. Locally both TACE and ablation would be considered in PS1 patients

Performance Status Test (PST) in cancer patients	
0	Normal activity
1	Some symptoms, near full ambulatory
2	Some symptoms, < 50% time in bed
3	Some symptoms, > 50% time in bed
4	Bedridden

HAP (Hepatoma Arterial Embolisation Prognostic) score:
Alb < 36g/dl (1 point), AFP > 400 ng/ml (1 point), Bil > 17 umol/l (1 point), Max TU diam > 7cm (1 point)
Median survival: HAP A (0) 27.6 mths, HAP B (1) 18.5 mths, HAP C (2) 9mths, HAP D (>2) 3.6 mths
When revalidated just in BCLC intermediate stage B patients median survival was 25.7, 18.5, 12.5 and 10 months for HAP A/B/C/D. HAP A and B patients are ideal for TACE, while C are equivocal.

Surveillance post treatment:
Irrespective of the treatment modality patients have a CT or MRI scan 4-6 weeks post treatment. If that shows a complete response then secondary surveillance involves a CT or MRI every 3-4 months for the first 2 years and then CT or MRI every 6 months for the next 3 years.

Further reading:

- Surveillance of cirrhosis for hepatocellular carcinoma: systematic review and economic analysis. Thompson-Coon et al. Health technology assessment 2007
- EASL Clinical Practice Guidelines. Management of Hepatocellular carcinoma 2018
- AASLD Practice guideline. Management of Hepatocellular cancer: 2018

Reference Number CG-GASTRO/2015/197	**Version:** 3		**Status** Final	Final
Version / Amendment History	Version	Date	Author	Reason
	3	2022	Liver Management Group	Previous guideline expired
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