Hepatocellular Carcinoma Screening & Treatment: Who, What, Why, & How?

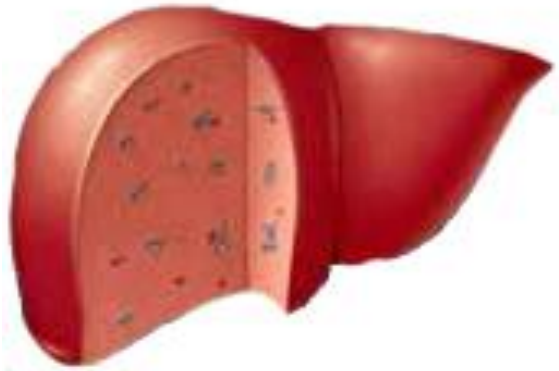
Kelleah Powao, NP
Texas Liver Institute
San Antonio

What is Hepatocellular Carcinoma (HCC)?

- Primary liver cancer
  - Originates from the hepatocytes
    - Other liver cancers, like cholangiocarcinoma, arise from other types of cells in the liver
- The development of HCC is initiated by
  - Hepatic injury → inflammation → necrosis of hepatocytes → regeneration
- This chronic liver disease sequentially transitions
  - Fibrosis → cirrhosis → hepatocellular carcinoma

Cirrhosis is the Final Common Pathway of All Chronic Liver Diseases

Normal Liver



Hepatitis C

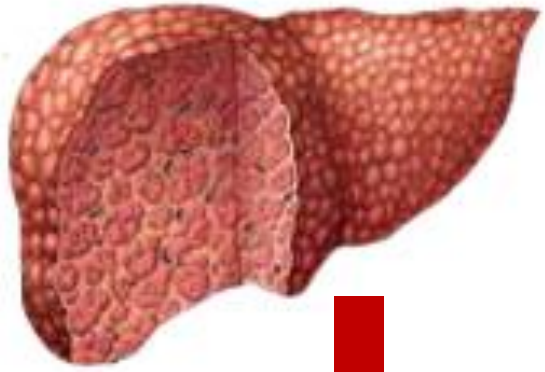
Alcohol use

Non-alcoholic fatty liver disease

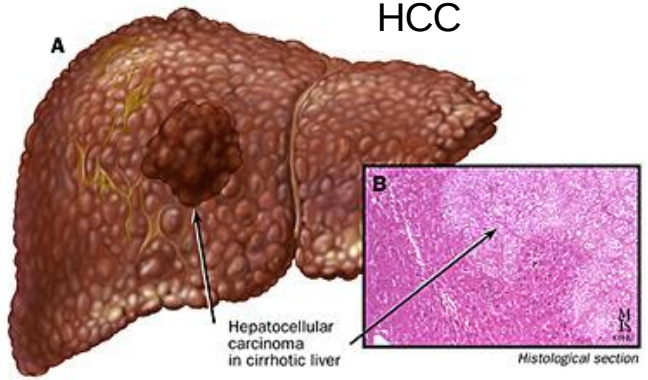
Hepatitis B

Other chronic liver diseases
(hemochromatosis, Wilson,
A1AT, autoimmune hepatitis, PBC, PSC)

Cirrhosis

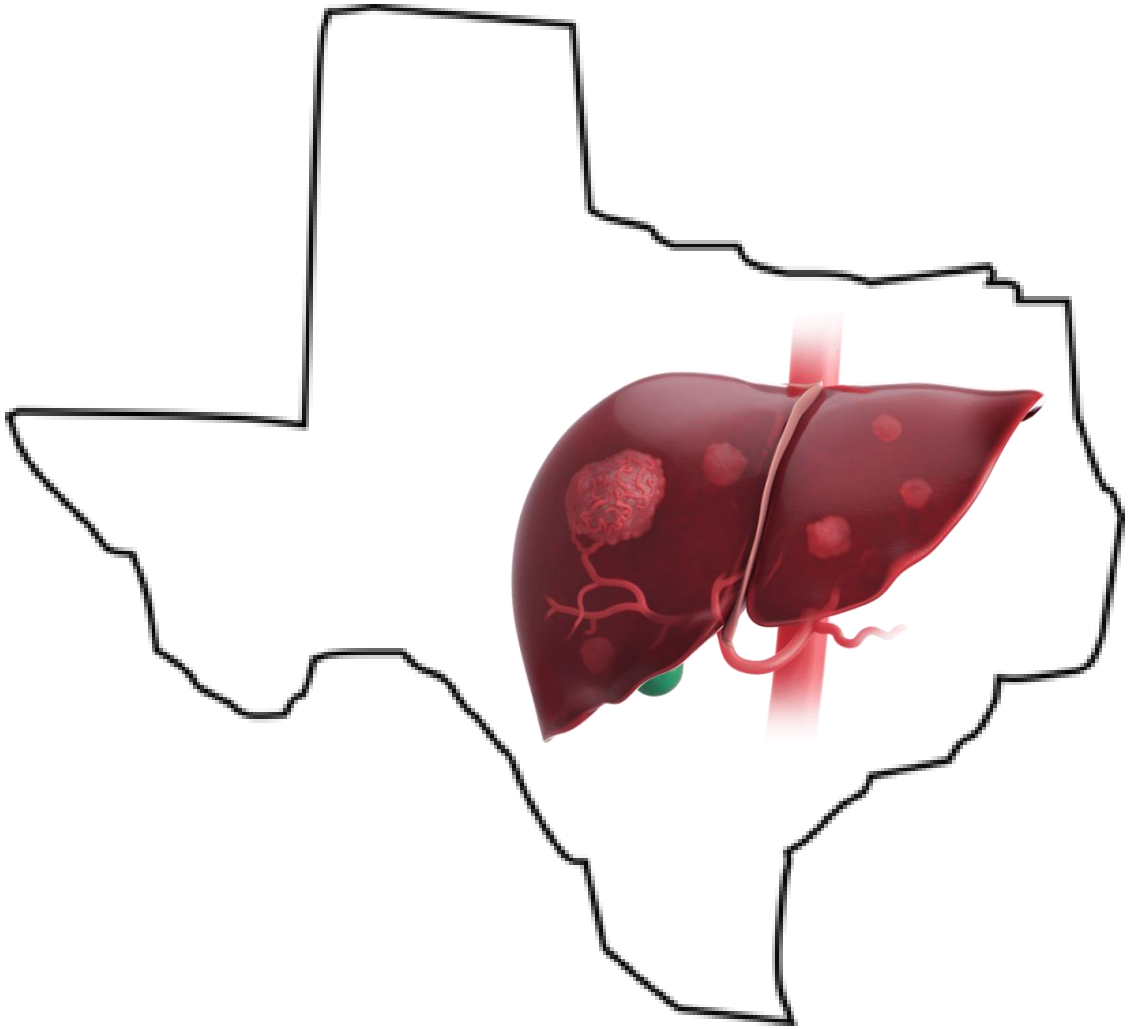


HCC

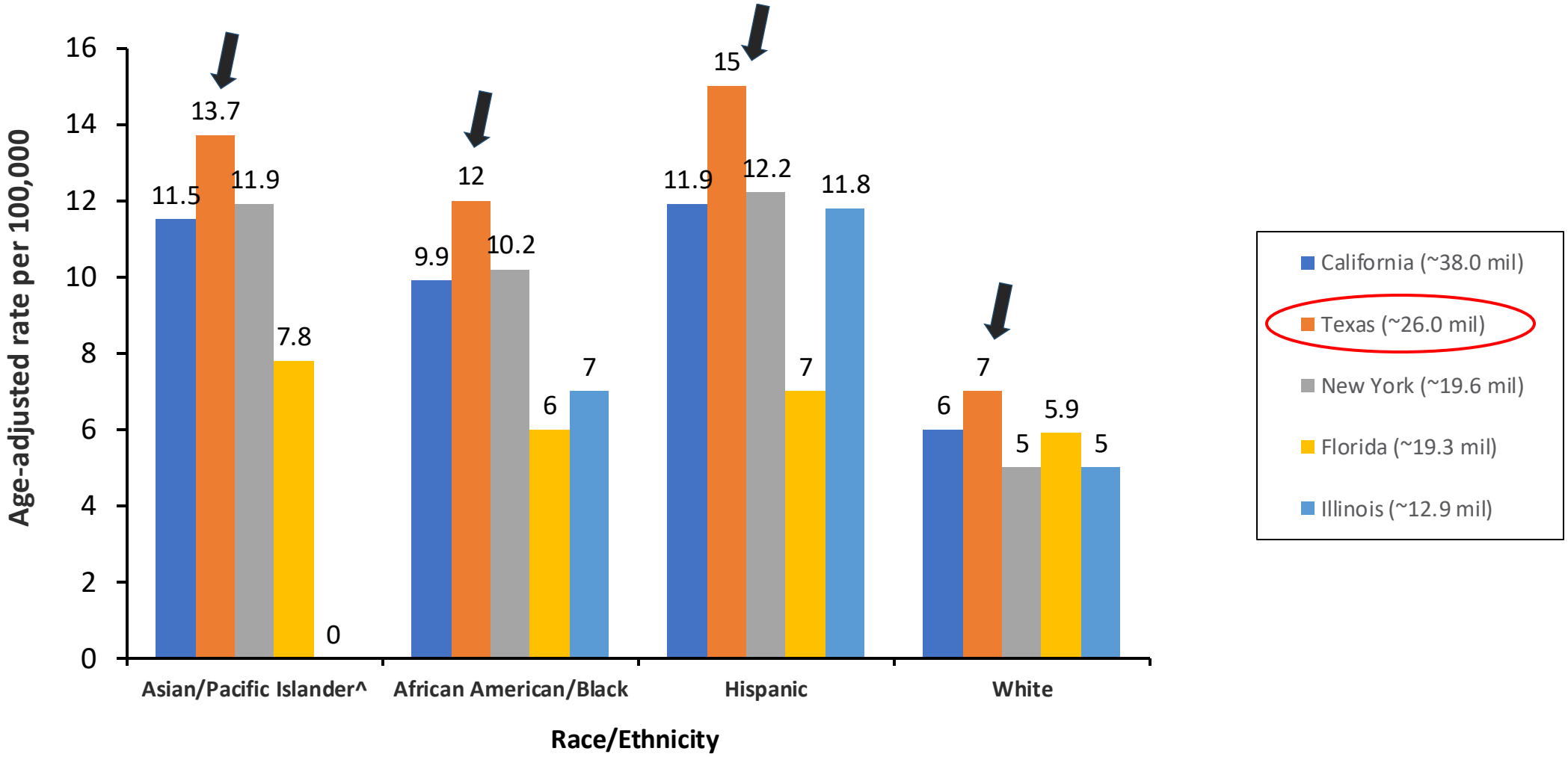


Why Should We Screen for HCC?

- 6th most common cancer worldwide
- 3rd leading cause of cancer-related death in both US & worldwide
- **Texas has the highest rate of HCC across all ethnicities!**



In the US, Texas has Highest Rate of HCC Across All Ethnicities



Who is at Risk?

Disease States

- Cirrhosis (~80%)
  - Alcohol
  - MASH
- Chronic Hepatitis B
- Chronic Hepatitis C

Patient Factors

- Males
- Family history of HCC
- Smoker
- Endemic country such as Asia or Sub-Saharan African
- American Indian, Hispanic, Black

Who Should We Screen?

Population group	Incidence of HCC
Sufficient risk to warrant surveillance	
Child-Pugh A–B cirrhosis, any etiology Hepatitis B Hepatitis C (viremic or post-SVR) Alcohol associated cirrhosis Nonalcoholic steatohepatitis Other etiologies	≥1.0% per year
Child-Pugh C cirrhosis, transplant candidate	
Non-cirrhotic chronic hepatitis B Man from endemic country[a] age >40 y Woman from endemic country[a] age > 50 y Person from Africa at earlier age[b] Family history of HCC PAGE-B score ≥ 10[c]	≥0.2% per year
Insufficient risk and in need of risk stratification models/biomarkers	
Hepatitis C and stage 3 fibrosis	< 0.2% per year
Noncirrhotic NAFLD	

New Threat: Non-cirrhotic MASLD

- MASLD is currently the **fastest growing** cause of HCC in liver transplant (LT) candidates
- MASLD has also become the leading cause of HCC in the absence of cirrhosis
  - ~25-33% of MASLD-related HCC occurs in the **absence of cirrhosis**
- Further data still needed to identify which patients with noncirrhotic MASLD have sufficient risk to warrant HCC surveillance
  - Currently, AASLD recommends against routine HCC surveillance in patients with MASLD who have advanced fibrosis but without cirrhosis (Level 3, Weak Recommendation)

Ioannou 2021, Loomba et al 2020, Kanwal et al 2018, Tan et al 2022

Cofactors for HCC

- Smoking is associated with a 20%–86% increased risk of HCC
  - Can return nearly to baseline after 30 years of smoking cessation
- Alcohol as a cofactor with other etiologies increases HCC risk 5-fold
- Obesity is associated with a 1.5–4.5x higher risk of HCC
- Metabolic syndrome, including diabetes, nearly doubles HCC risk in the absence of overweight/obesity
- Dietary exposure to aflatoxin B1 and aristolochic acid are known cofactors for HCC in patients with HBV infection

What are the Symptoms of HCC?

- Clinical Presentation
  - Asymptomatic early stages
  - Decompensation event
  - Jaundice
  - Weight loss
  - Abdominal pain

How to Screen for HCC?

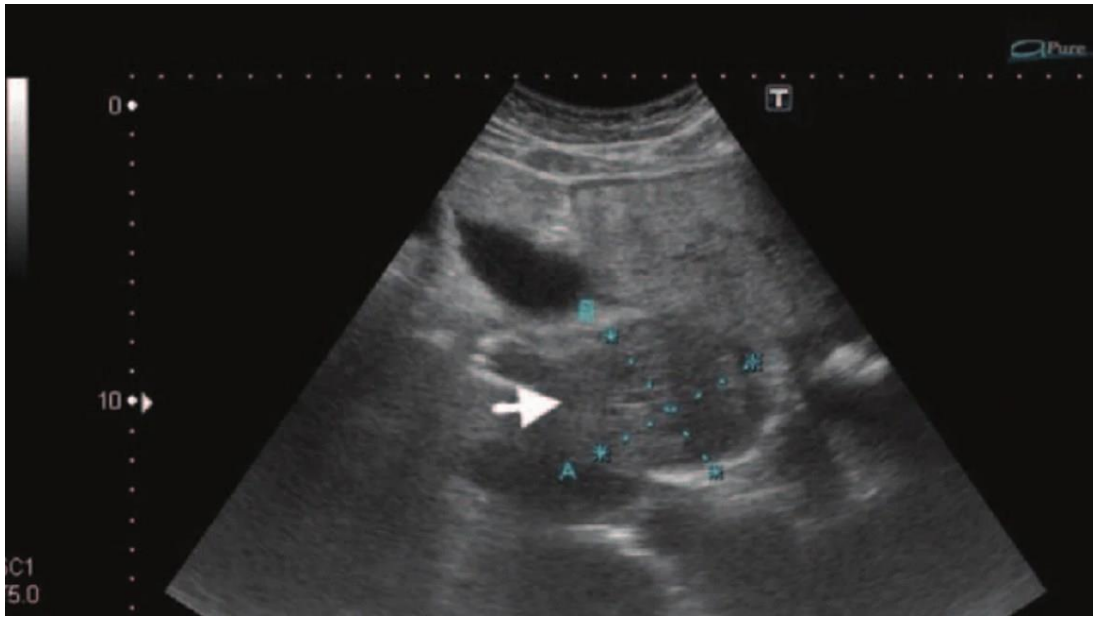
- Surveillance Guidance
  - American Association for the Study of Liver Diseases (AASLD)
  - European Association for the Study of the Liver (EASL)
- Risk-based approach
  - Cirrhosis
  - Chronic HBV

American Association for the Study of Liver Diseases[10,21]	US every 6 months
European Association for the Study of the Liver[39]	US every 6 months
Asian-Pacific Association for the Study of the Liver[38]	AFP + US every 6 months
National Comprehensive Cancer Network[40]	AFP + US every 6-12 months
US Department of Veterans Affairs[41]	AFP + US every 6-12 months

AFP, alpha-fetoprotein; HCC, hepatocellular carcinoma; US, ultrasonography.

HCC Surveillance

- **Ultrasound + AFP every 6 months**
- Screening Tools
  - Ultrasound:
    - Sensitivity, specificity
  - Alpha-fetoprotein (AFP):
    - Limitations and utility
  - Imaging (CT, MRI):
    - When and why to use advanced imaging
    - Contrast

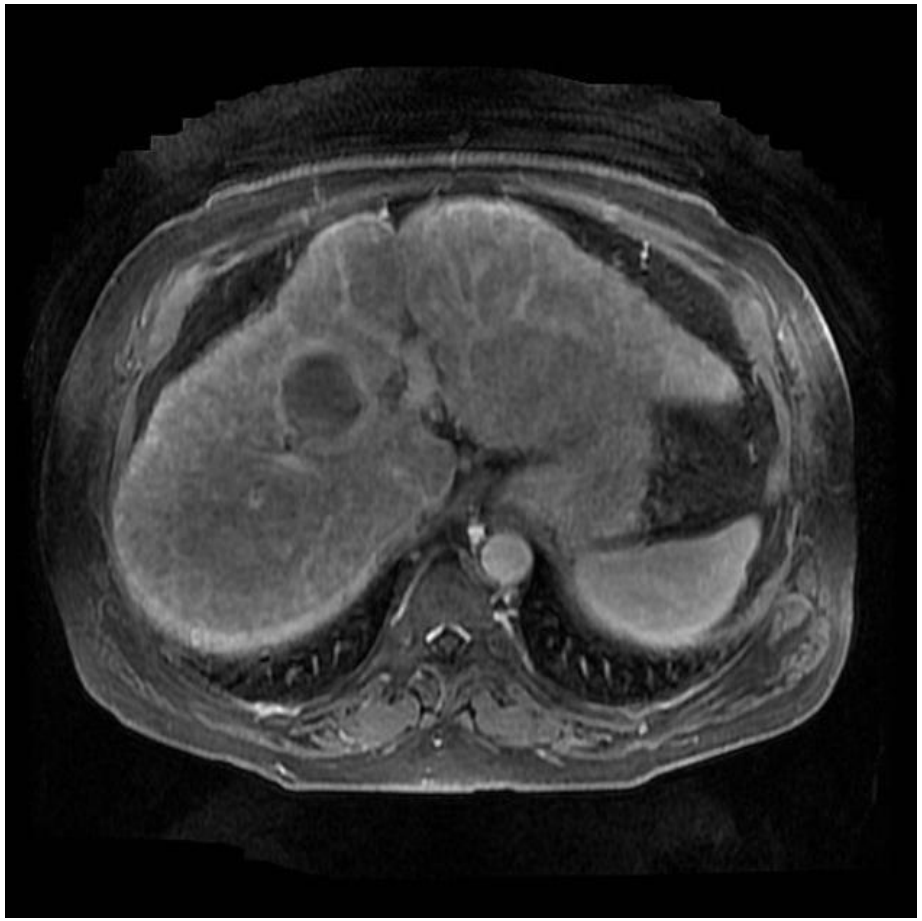


Why Check for HCC Every 6 Months?

- Recommendation initially based off the “doubling time” of HCC
- Importance of early detection
  - Improved prognosis and survival rates
  - More treatment options
  - Better liver function preservation
  - Prevention of cancer progression

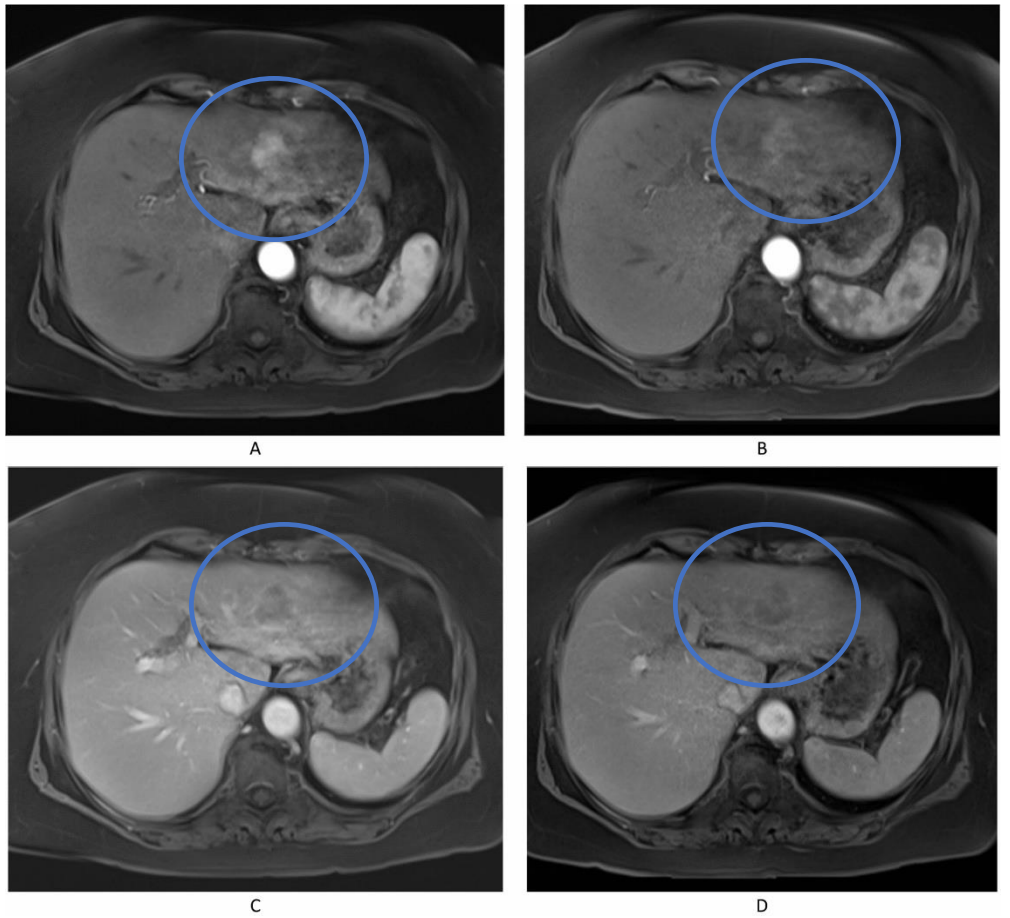
Lesion on Ultrasound – Now What?

- Contrast-enhanced, multiphase imaging!
  - MRI abd w/wo
  - CT abd w/wo
  - A recent meta-analysis suggests MRI has higher sensitivity (82% vs 66%), with similar specificity (92% vs 91%) vs CT for diagnosing HCC
- Unlike most cancers, the diagnosis of HCC can be established in at-risk patients based on specific noninvasive imaging criteria **without need for histologic confirmation**
  - LIRADS



LIRADS

- Radiological hallmarks of HCC on contrast multiphase imaging
  - Arterial phase hyperenhancement (APHE)
  - Washout on portal venous or delayed phases
- High specificity and positive predictive value in lesions ≥1 cm

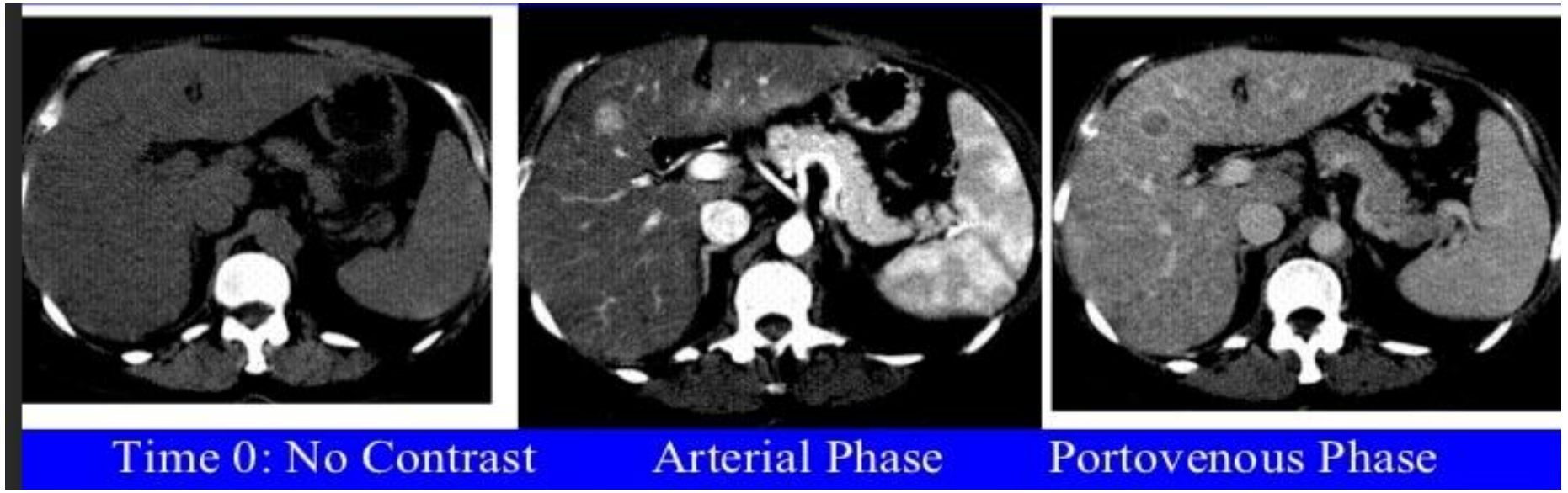


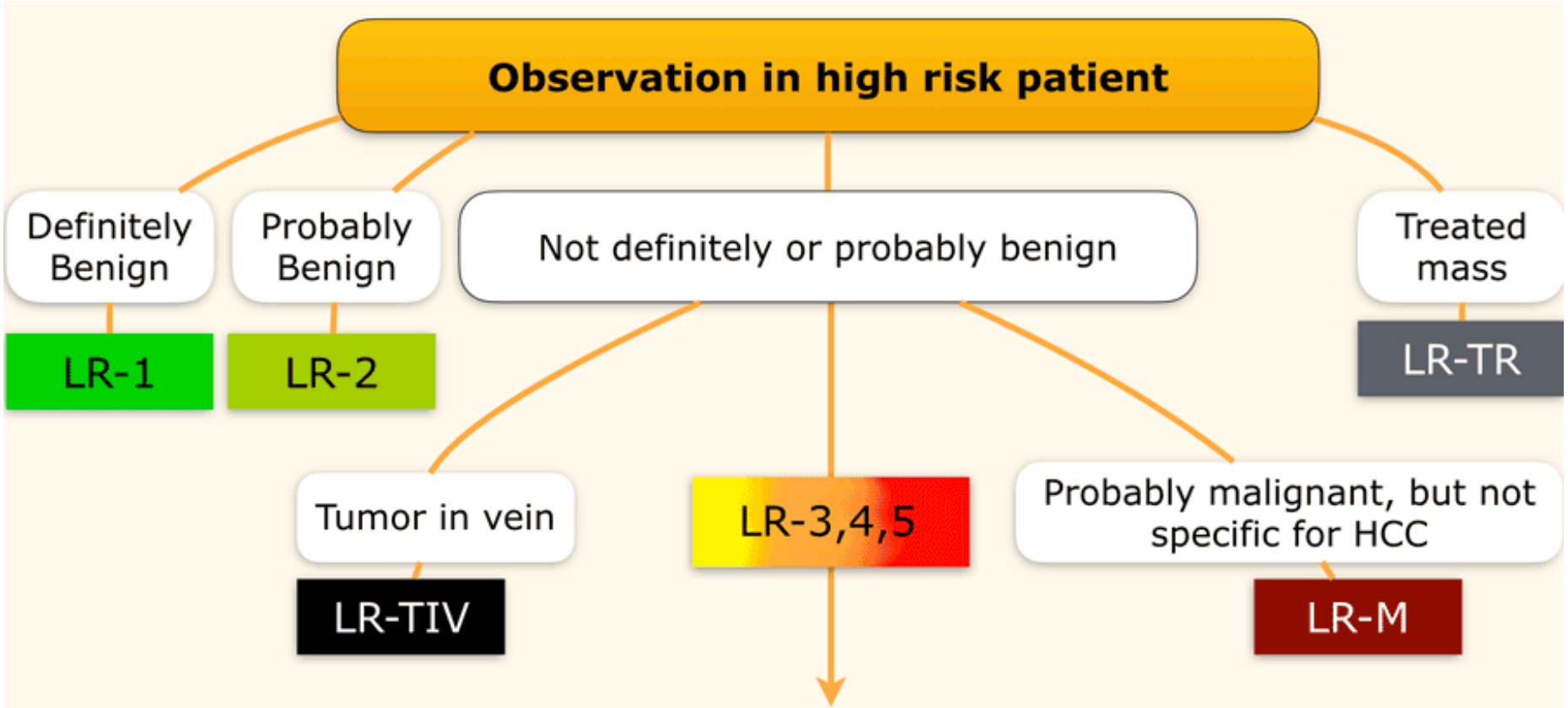
Diagnosis

IMPRESSION:

1. Arterially enhancing exophytic left hepatic lesion measuring 2.1 cm with delayed phase washout on pseudocapsular enhancement concerning for HCC (LR-5).

2. Cirrhotic liver without evidence of portal hypertension





	Arterial phase hypo- or iso- enhancement		Arterial phase non-rim hyperenhancement		
Size in mm	<20	≥20	<10	10-19	≥20
none	LR3	LR3	LR3	LR3	LR4
one	LR3	LR4	LR4	LR4* / LR5	LR5
≥two	LR4	LR4	LR4	LR5	LR5

Enhancing capsule
Non-peripheral washout
Threshold growth

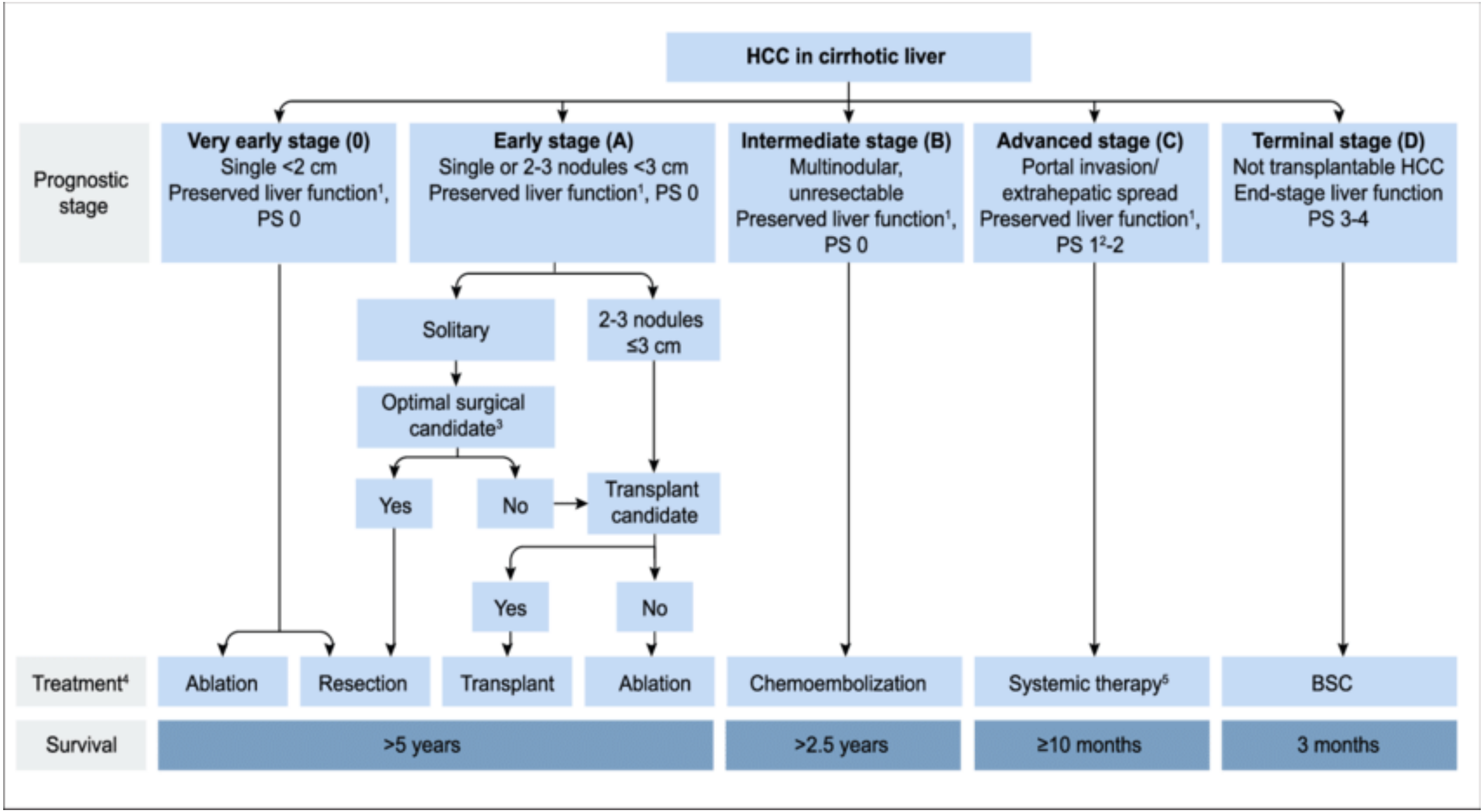
What are the Treatment Options for HCC?

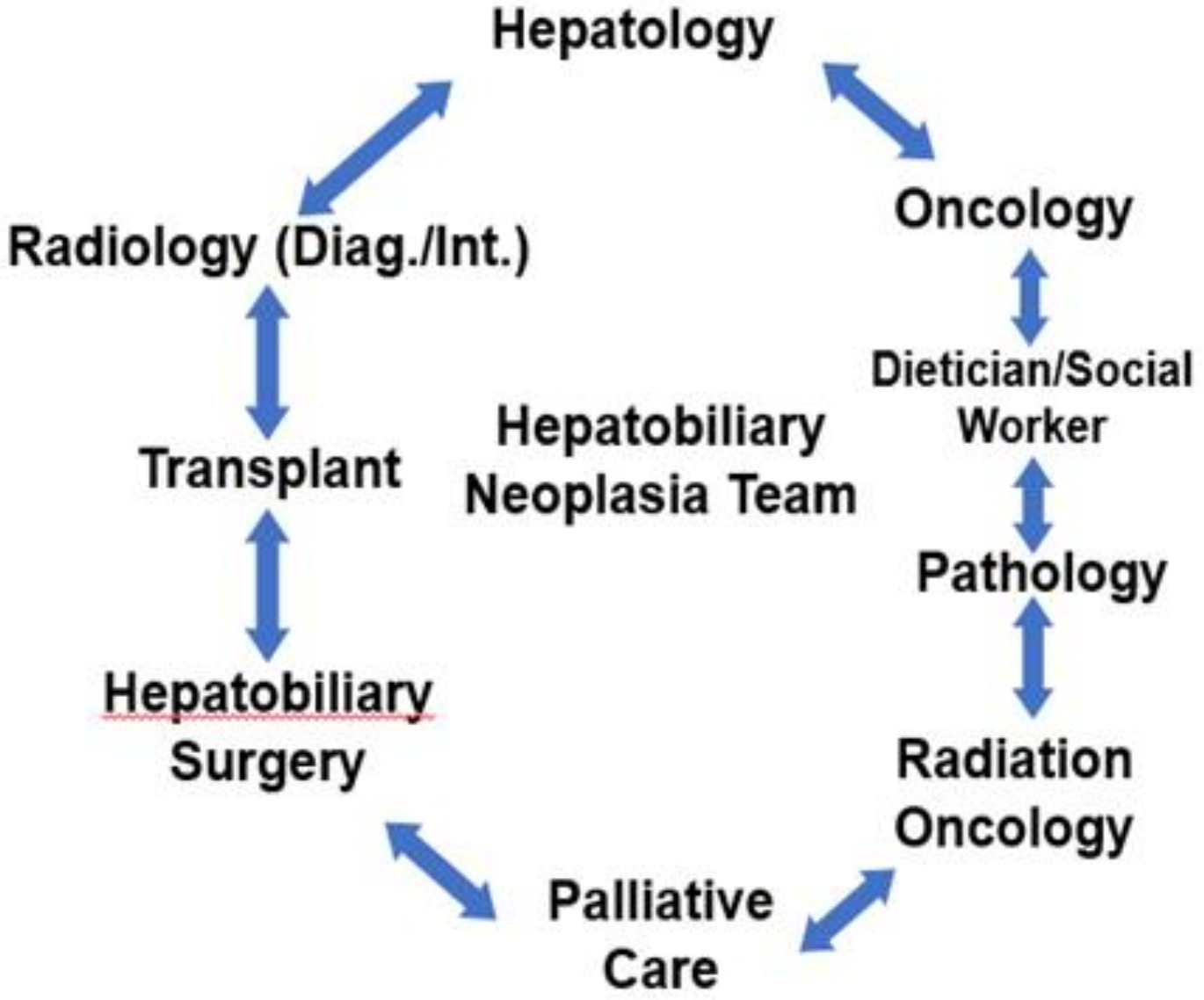
- Curative treatments
  - Surgical resection
    - Indications, outcomes
    - Implications for liver transplant
  - Liver transplantation
    - Criteria, Outcomes, limitations
- Locoregional therapies
  - RFA, MWA, TACE, Y90, SBRT
- Systemic therapy
  - Targeted therapies: e.g. sorafenib, atezolizumab, bevacizumab, cabozantinib, lenvatinib
  - Immunotherapy: e.g. checkpoint inhibitors

COMBO THERAPY

How to Decide on Treatment?

- Staging systems
  - Barcelona Clinic Liver Cancer (BCLC) staging
  - Milan criteria
  - Child-Pugh classification for liver function
- Factors influencing treatment choice
  - Tumor size, location, number
  - Liver function
  - Performance status of patient


HCC in cirrhotic liver
Prognostic stage
Very early stage (0)
Single <2 cm
Preserved liver function[1], PS 0
Early stage (A)
Single or 2-3 nodules <3 cm
Preserved liver function[1], PS 0
Intermediate stage (B)
Multinodular, unresectable
Preserved liver function[1], PS 0
Advanced stage (C)
Portal invasion/ extrahepatic spread
Preserved liver function[1], PS 1[2]-2
Terminal stage (D)
Not transplantable HCC
End-stage liver function
PS 3-4
Solitary
2-3 nodules ≤3 cm
Optimal surgical candidate[3]
Yes
No
Transplant candidate
Yes
No
Treatment[4]
Ablation
Resection
Transplant
Ablation
Chemoembolization
Systemic therapy[5]
BSC
Survival
>5 years
>2.5 years
≥10 months
3 months



Multidisciplinary Care is Critical

Emerging Trends in HCC Management

Advances in Early Detection

- Liquid biopsy & Genetic Biomarkers
- Analyzing imaging with AI and machine learning

Innovative Treatment Options

- Multidisciplinary tumor board
- LDLT
- Gene and cell-based therapies

Key Takeaways

- Risk factors for HCC: HBV, HCV, cirrhosis, MASH, DM, ETOH, aflatoxin
- High-risk patients and patients with cirrhosis need HCC screening with US + AFP every 6 months
- Liver lesions are best evaluated by contrast-enhanced multiphase imaging such as MRI abd w/wo
- Hepatocellular carcinoma can usually be diagnosed radiographically without biopsy
- Patients should be referred for evaluation by a multidisciplinary team including hepatology, transplant surgery, IR, oncology, etc.
- Liver transplant can be a cure for liver cancer!