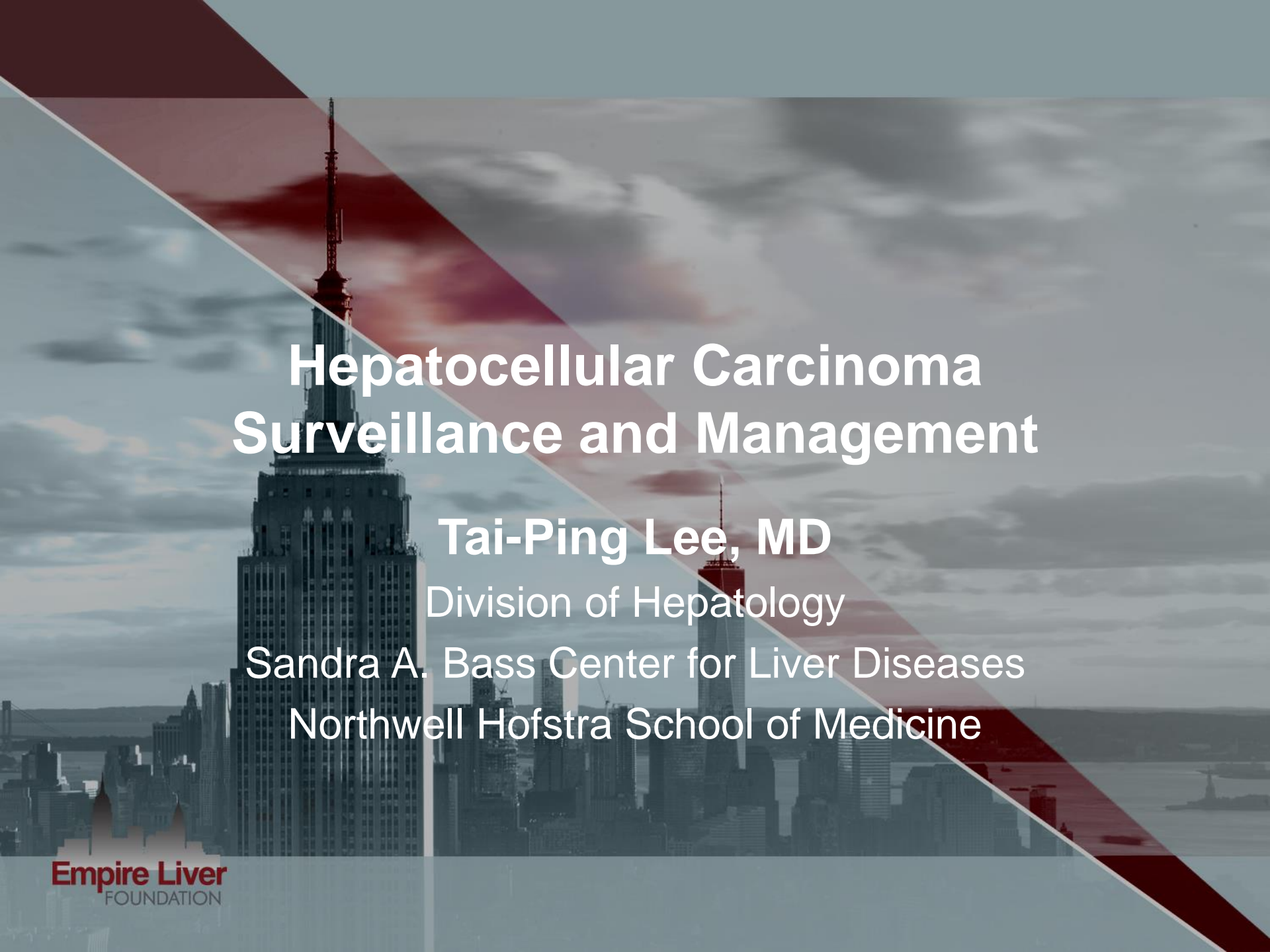




NEW YORK STATE
HCV PROVIDER
CLASSIFICATION TRAINING



Hepatocellular Carcinoma Surveillance and Management

Tai-Ping Lee, MD

Division of Hepatology

Sandra A. Bass Center for Liver Diseases

Northwell Hofstra School of Medicine

Objectives

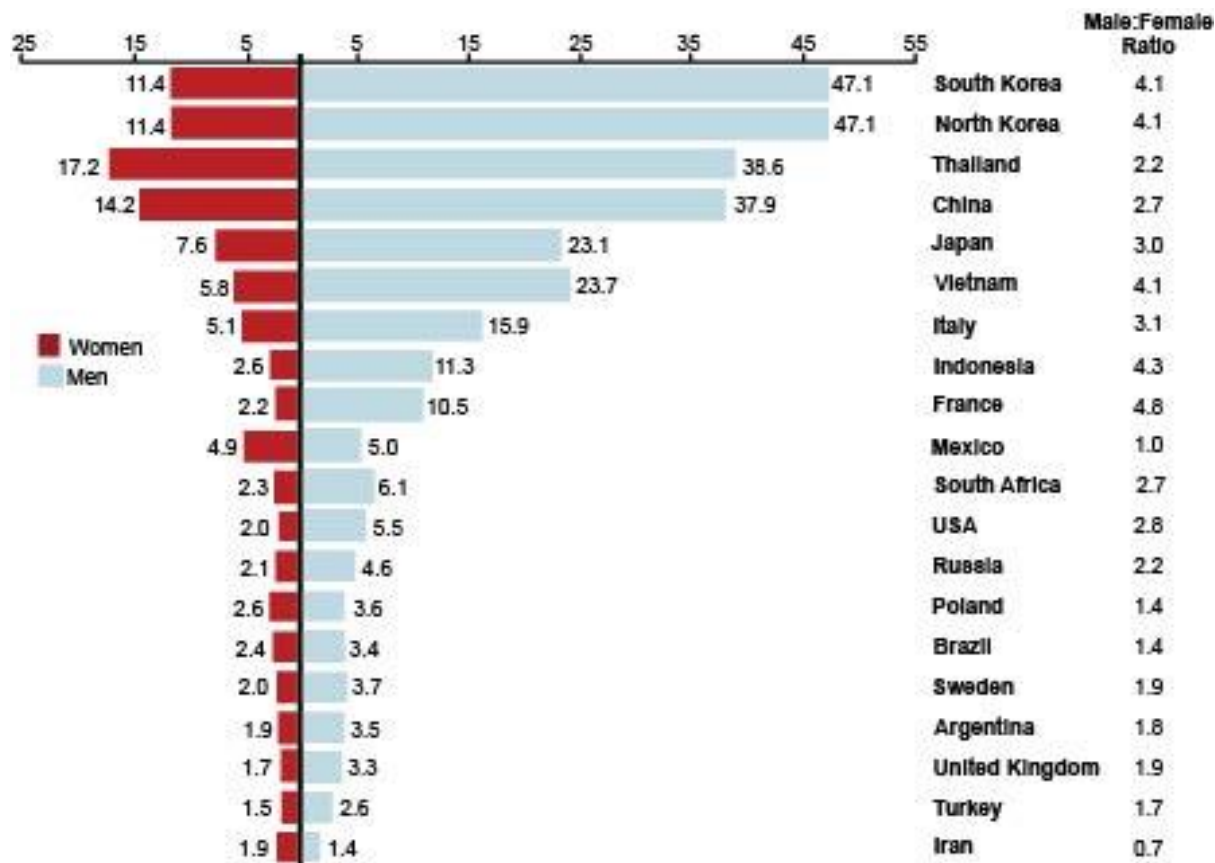
By the end of this presentation, learners should be able to

1. Describe risk factors for developing HCC
2. Describe surveillance for HCC in patients at risk.
3. Describe the impact of screening for HCC on survival.
4. Describe diagnostic modalities for HCC.

Surveillance for Hepatocellular Carcinoma (HCC)

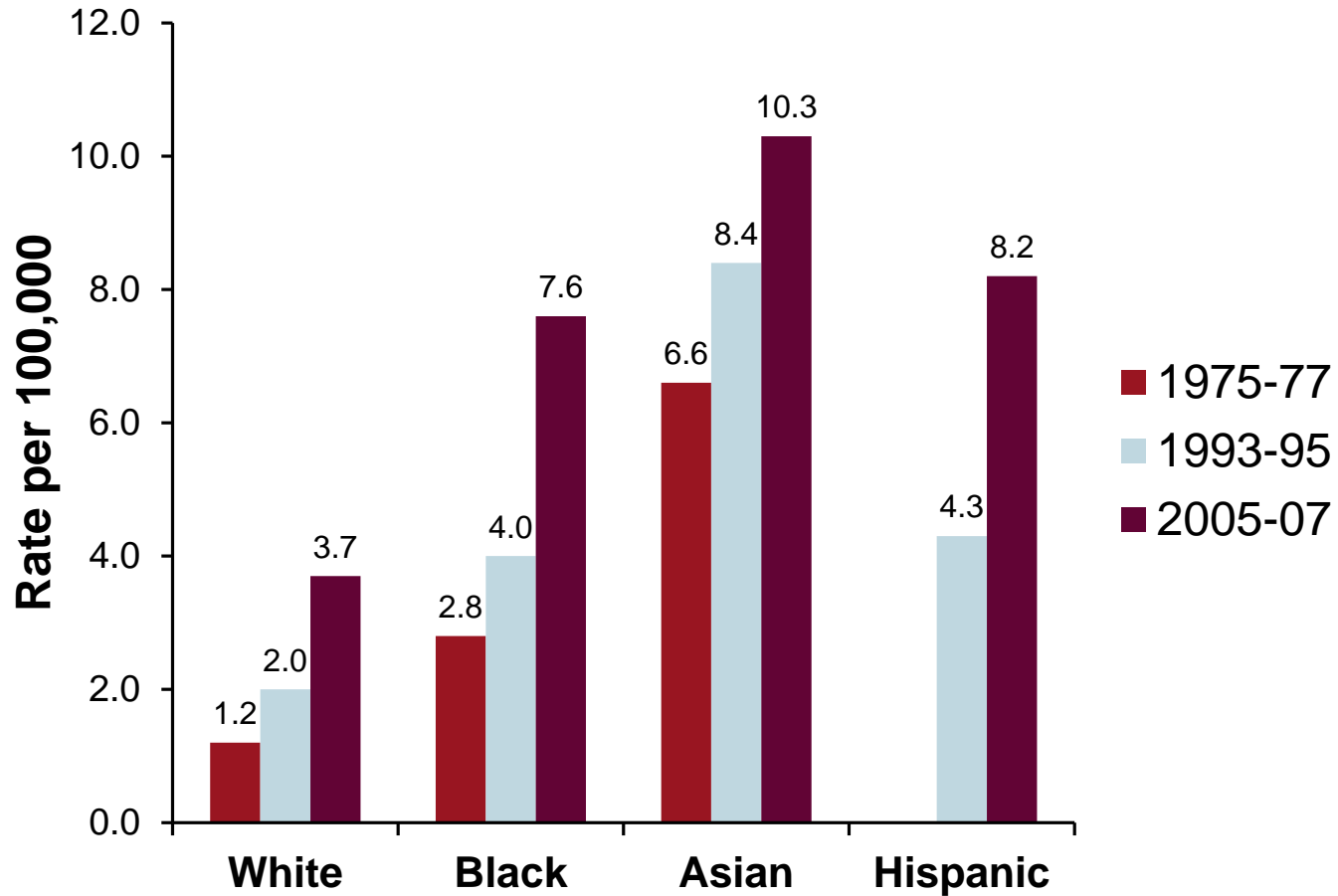
- Screening
 - Application of diagnostic tests in patients at risk for HCC in whom no prior reason to suspect that HCC is present.
- Surveillance
 - The repeated application of screening tests.

Age-Standardized Incidence Rates of Liver Cancer

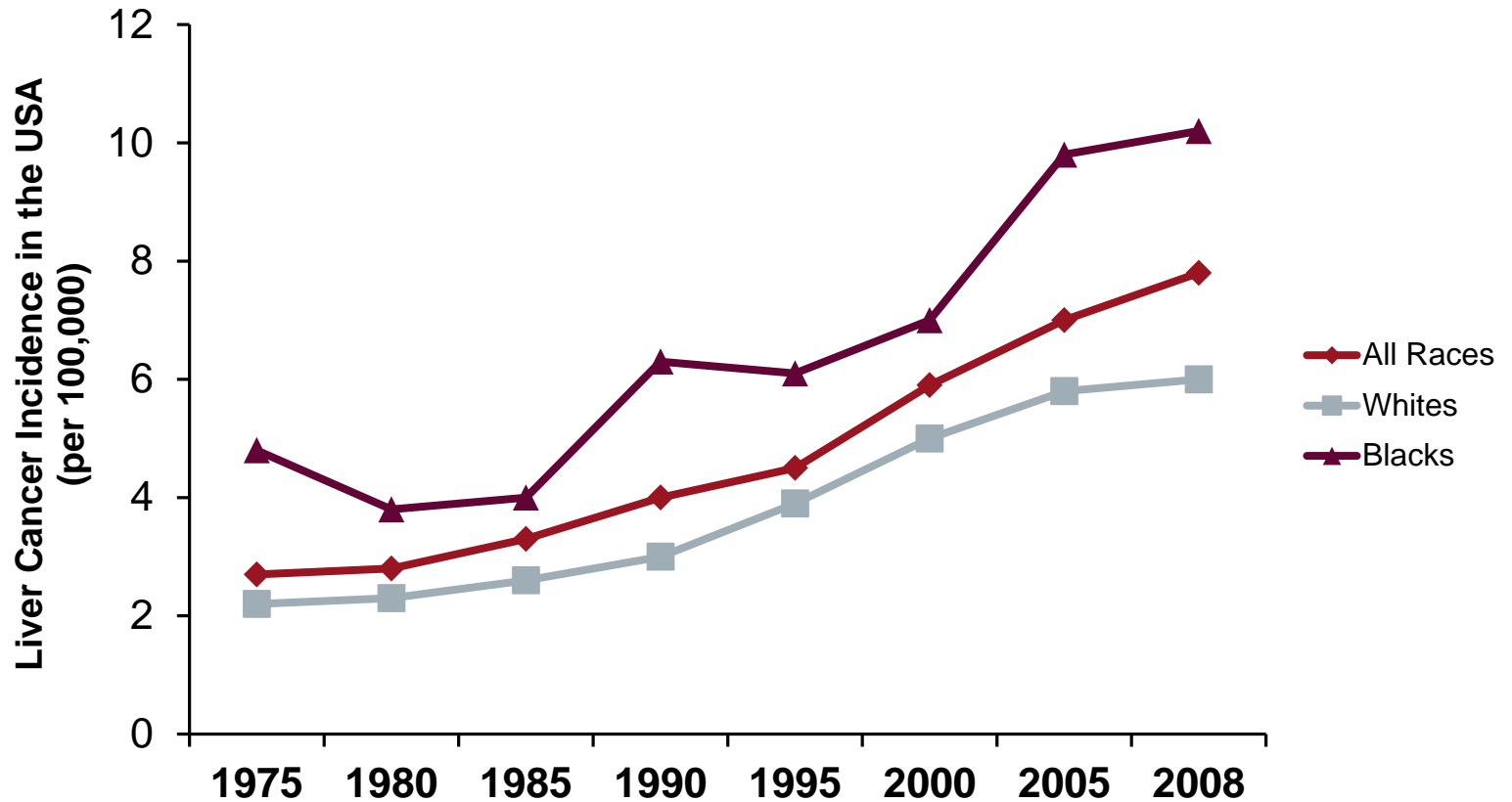


Age-standardized incidence rates of hepatocellular carcinoma per 100,000 populations at risk, in different regions of world (Source: GLOBOCAN 2002).

Incidence Rate of Hepatocellular Carcinoma by Race in the US

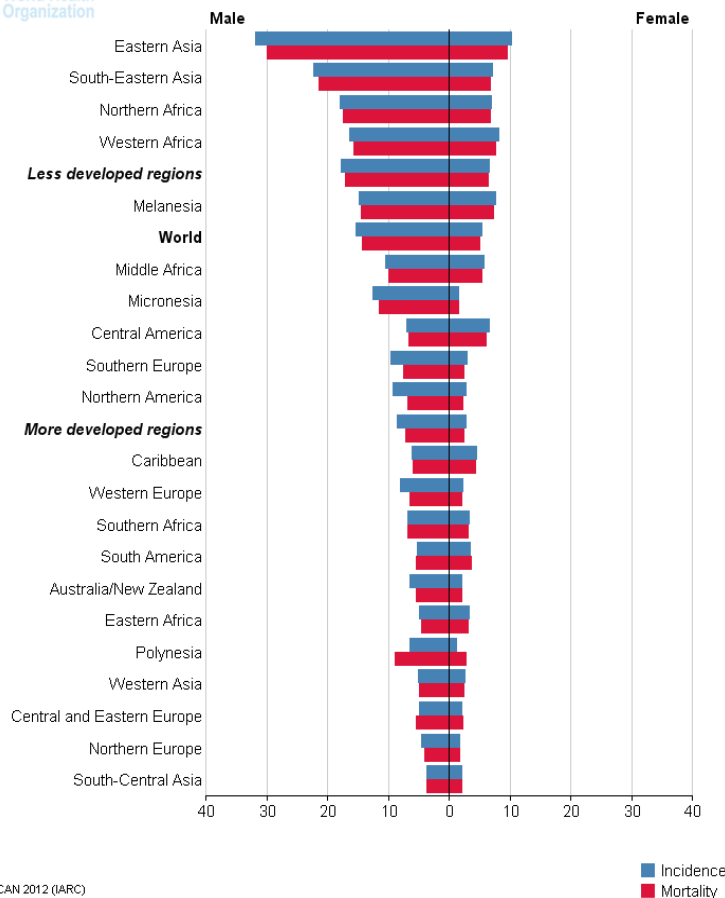


Age-Adjusted Incidence Rates of Liver Cancer in the US



Estimated Age-Standardized Rates per 100,000 Populations at Risk

International Agency for Research on Cancer



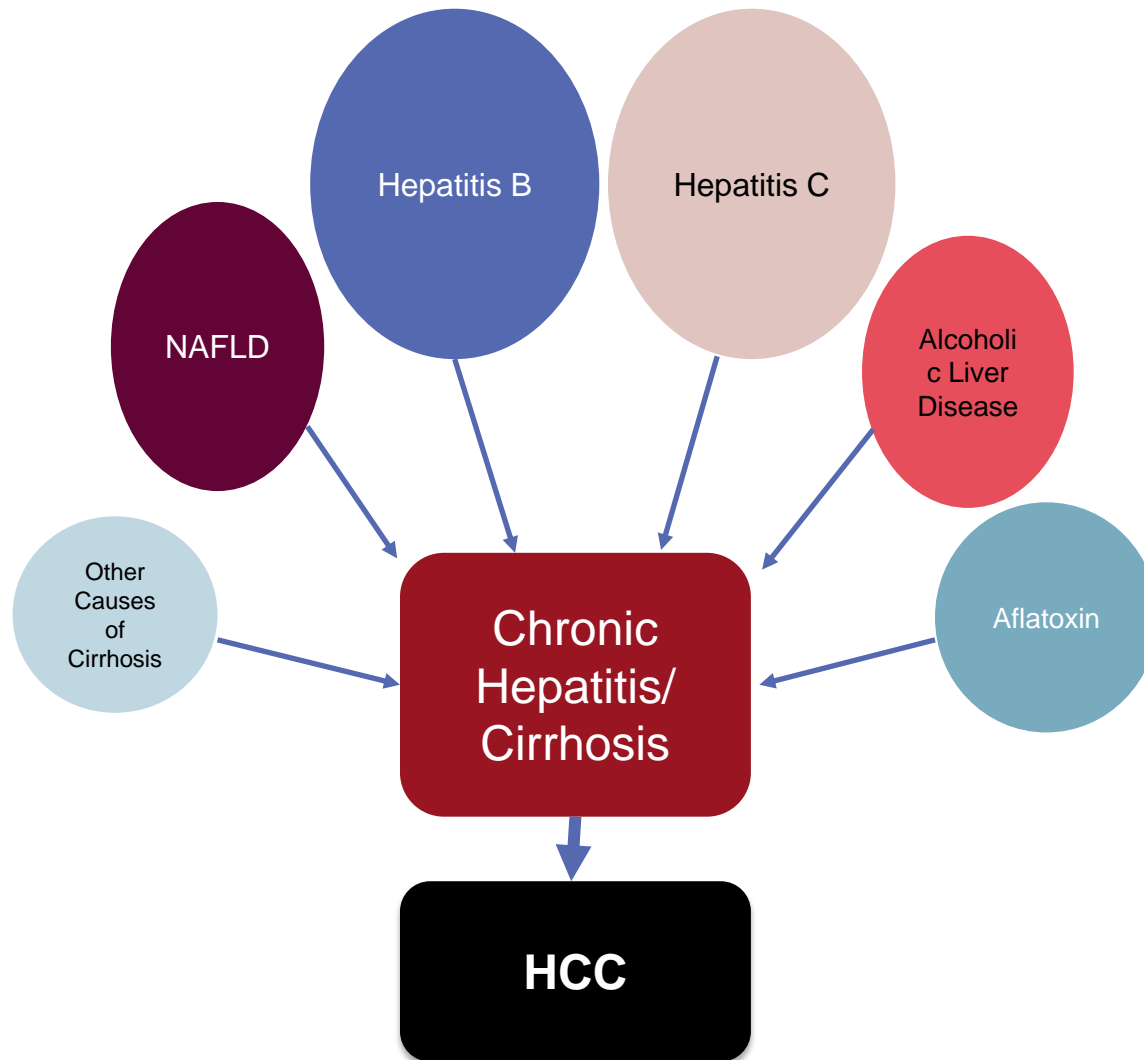
GLOBOCAN 2012 (IARC)

Estimated age-standardized rates (World) per 100,000 populations at risk, in different regions of world (Source: GLOBOCAN 2012).

Emerging Trends in HCC: Incidence and Mortality

- Liver cancer is the 2nd leading cause of cancer-related death in the world.
- HCC incidence and death rates are increasing in many parts of the world, including North America.
- In the US, HCC incidence rates increased by 3.1% per year from 2008 to 2012
- In the US, death rates from HCC in men increased by 2.8% per year and for women it increased by 3.4% per year.

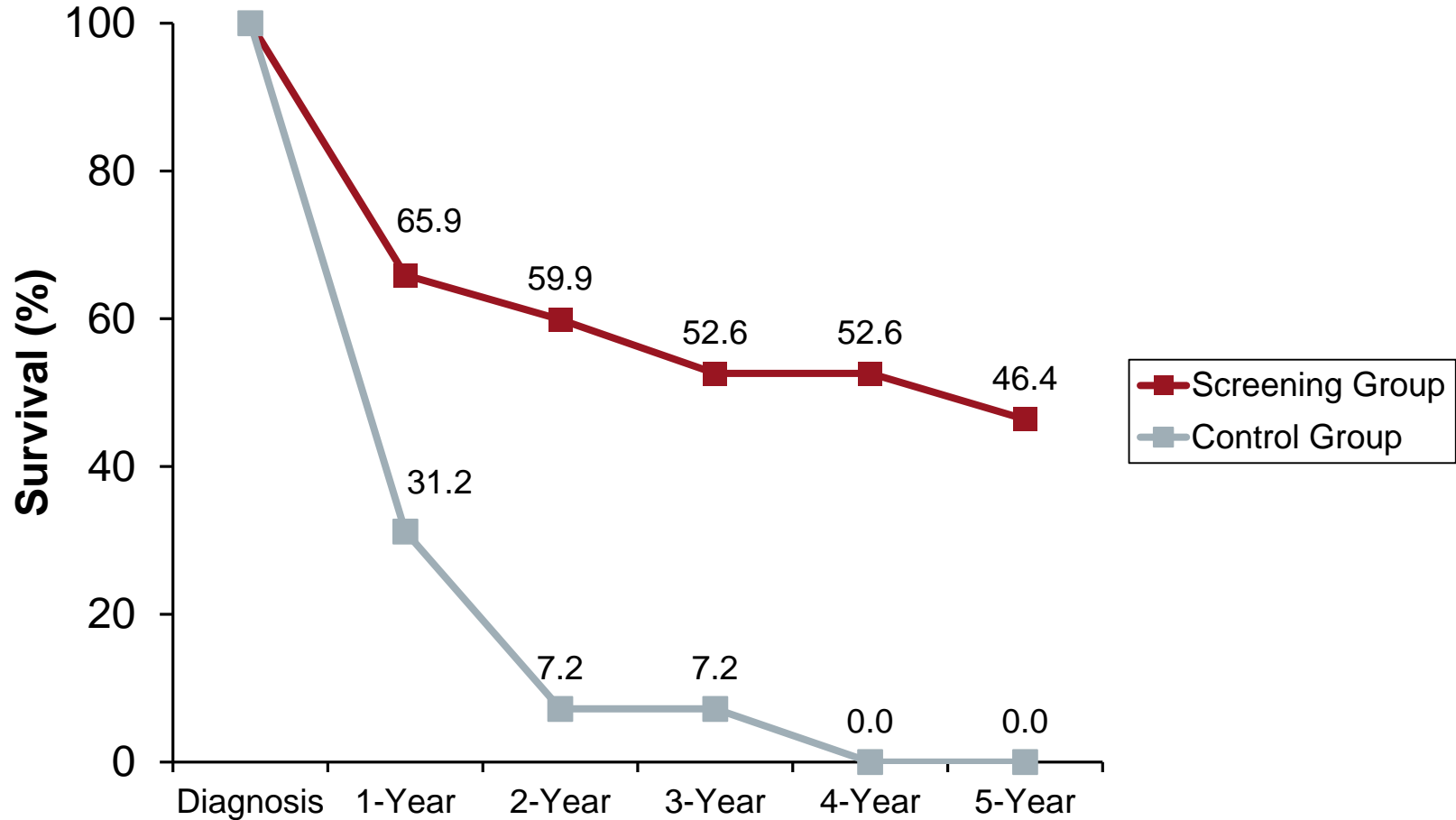
Risk Factors for Developing Hepatocellular Carcinoma



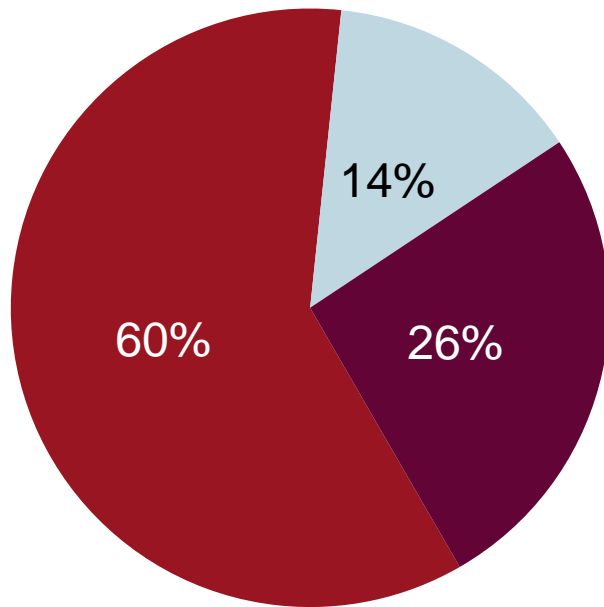
Surveillance for HCC

Cirrhosis secondary to	Screening for Chronic hepatitis B carriers without cirrhosis
Viral hepatitis (B, C)	Asian man over age 40
Primary biliary cholangitis	Asian woman over age 50
Genetic hemochromatosis	African over age 20
A1-antitrypsin deficiency	Family history of HCC
Non-alcoholic fatty liver disease	Any carrier older than age 40 with persistent or intermittent ALT abnormalities and/or HBV DNA > 2000 IU/ml
Other cause of cirrhosis	

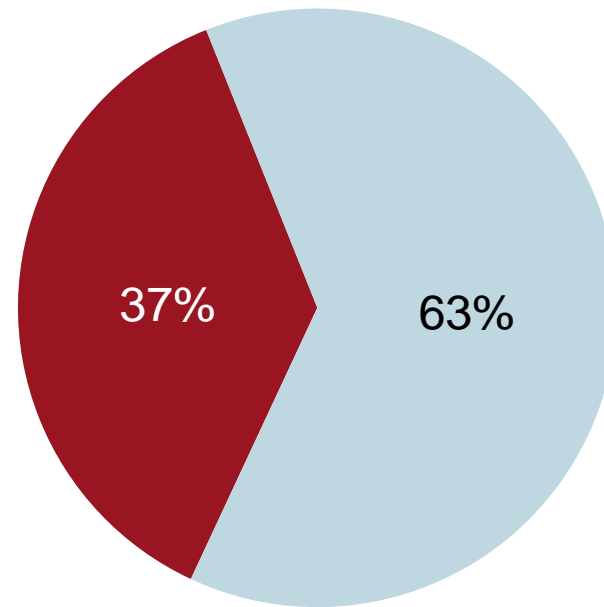
Impact of Screening on Survival After Diagnosis of HCC



Impact of Screening on Stage of HCC at Time of Diagnosis

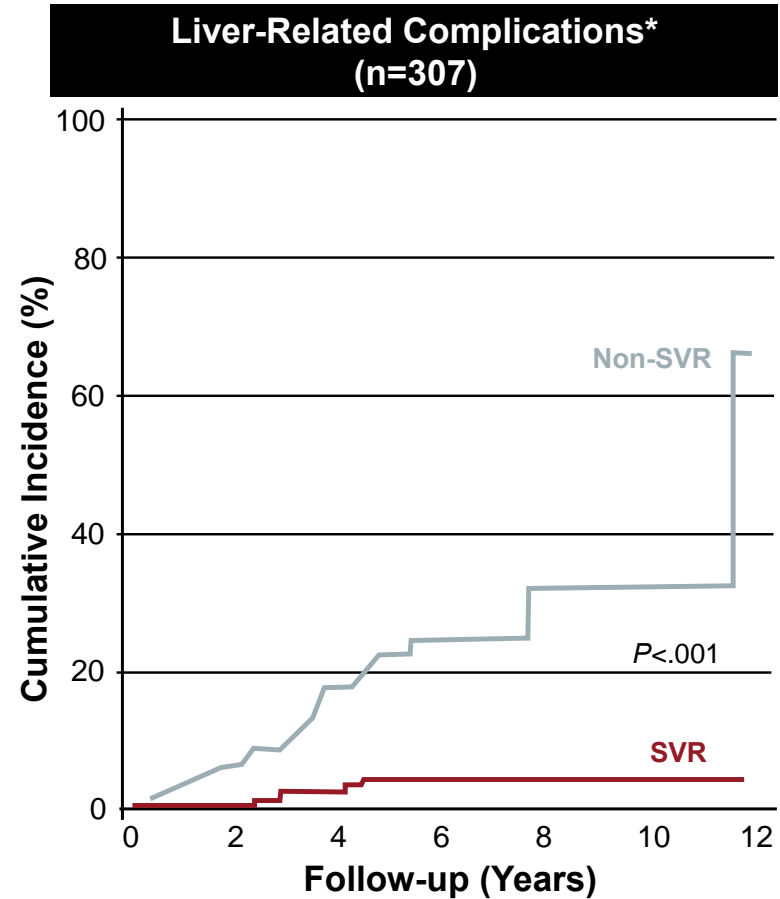
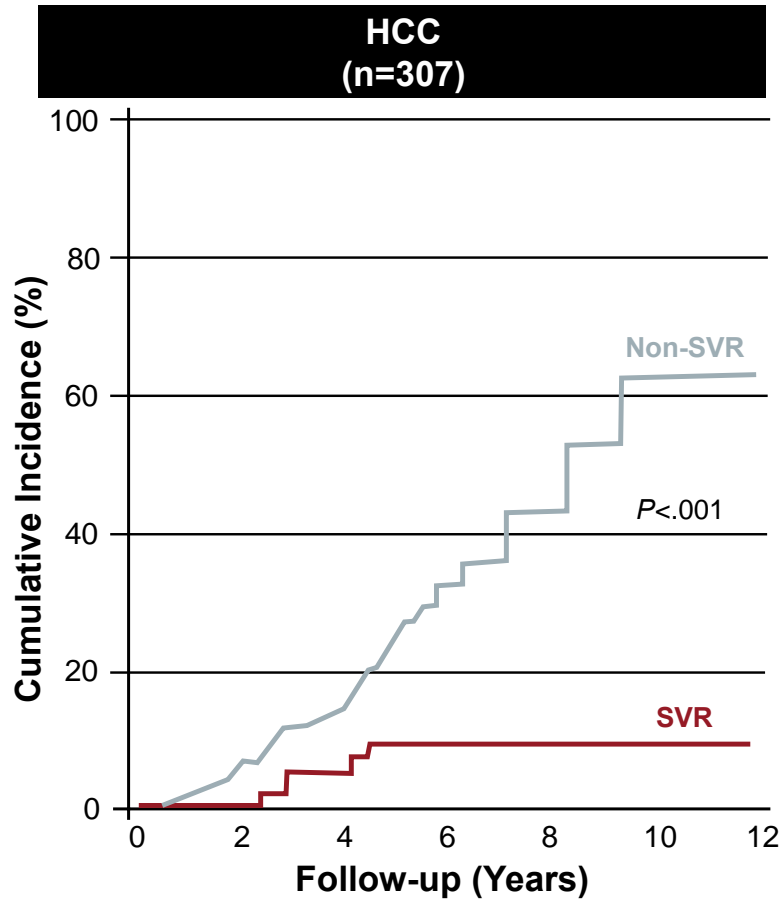


Screened Group



Control Group

SVR to HCV Therapy Reduced HCC and Liver-Related Complications in Patients with Bridging Fibrosis or Cirrhosis



*Ascites, variceal bleeding.

307 HCV patients with bridging fibrosis (n=127) or cirrhosis (n=180) were evaluated by Cox regression analysis.

Non-SVR in 67% of patients treated with pegylated interferon plus ribavirin. Median follow-up: 3.5 years.

Cardoso A-C, et al. *J Hepatol.* 2010;52:652-657.

Risk Factors for HCC Development Among SVR Patients with Cirrhosis

Study	SVR Patients with Cirrhosis	Median Follow-up (years)	# Incident HCC	Risk Factors
Van der Meer 2012	843 (84%)	6.7	50 (5%)	Age
Chang 2012	339 (38.9%)	3.5	37 (4.2%)	Age, F3-F4, AFP, thrombocytopenia
Arase 2013	149 (7.8%)	8.1	44 (2.3%)	Male, age, alcohol, diabetes
Huang 2014	86 (13.4%)	4.4	33 (5.1%)	Age, F4, GGT

Surveillance for HCC Post SVR

- SVR reduces HCC risk, but patients with fibrosis or cirrhosis remain at increased risk of HCC post SVR (annual incidence 0.5-2%).
- HCC risk persists for >10 years post SVR despite potential regression of fibrosis, surveillance may be needed indefinitely.
- HCC risk may plateau after first 6-7 years but unknown when falls below cost effectiveness threshold.
- Recurrence of HCC may increase post SVR.

Diagnosis of HCC

- Radiological diagnosis of HCC
- Role of AFP or serum markers
- Pathological diagnosis of dysplasia and early HCC

Ultrasound for HCC Surveillance

- Is not effective for surveillance of HCC in clinical practice (only 31.7% sensitive in early stage of HCC).
- Potential limitations of Ultrasound
 - Operator characteristics
 - Patient characteristics: obesity, liver echogenicity, ascites
- Improve effectiveness by better imaging quality, combining with biomarkers

CT Scan for HCC Surveillance

Variable	Ultrasound (N=83)	CT (n=80)	P-value
Number of HCC	9 (10.8%)	8 (10.0%)	0.86
Proportion BCLC A	5 (55.5%)	5 (62.5%)	0.93
HCC-related mortality	5 (6.0%)	7 (8.8%)	0.46
False positive imaging	3 (3.6%)	9 (5.6%)	0.06
Cost per HCC	\$17,041	\$57,383	

MRI for HCC Surveillance in Cirrhosis

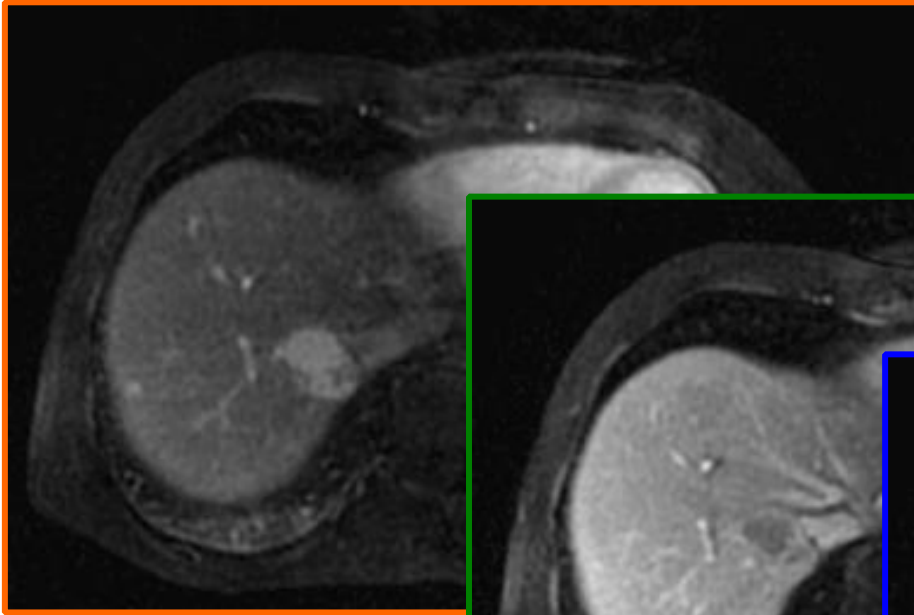
- Prospective cohort study with 407 Child A-B patients
 - 1112 surveillances performed over 1.5 years
 - US and MRI in all patients
- 35 patients with total of 40 HCC nodules
- 26 patients had BCLC stage 0 and 8 patients BCLC stage A

Cohort	MRI	US	P-value
Sensitivity	97%	40%	P < 0.001
Sensitivity for BCLC 0	96%	42%	P < 0.001
Specificity	94%	90%	P = 0.049

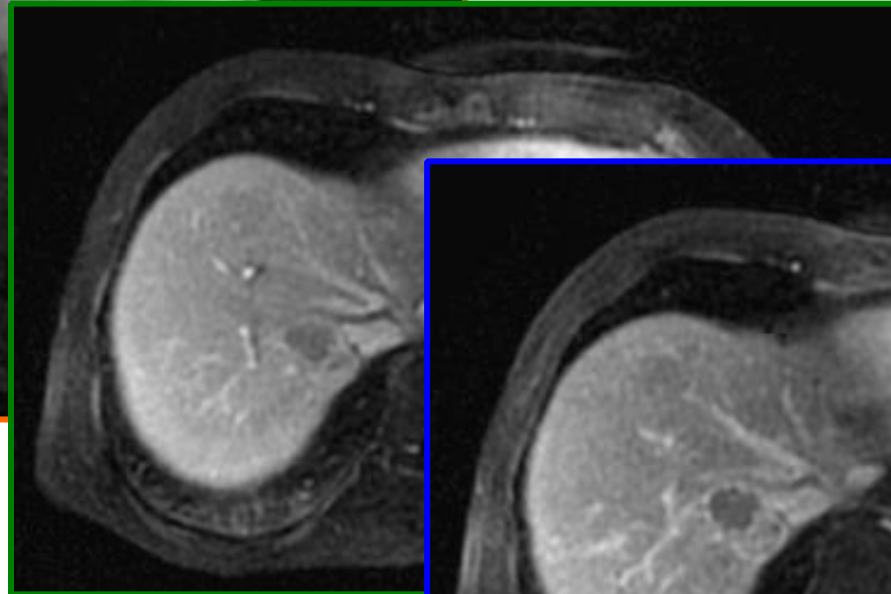
HCC Diagnosis Is Established by Imaging Criteria

- Intense contrast uptake in the arterial phase followed by contrast washout in the venous phase, and capsule is considered specific for HCC on MRI and CT.
- Nodules 1 cm or less may not be validated as tumor. Such nodules should be followed with serial studies.
- PET scans are not useful due to low sensitivity.

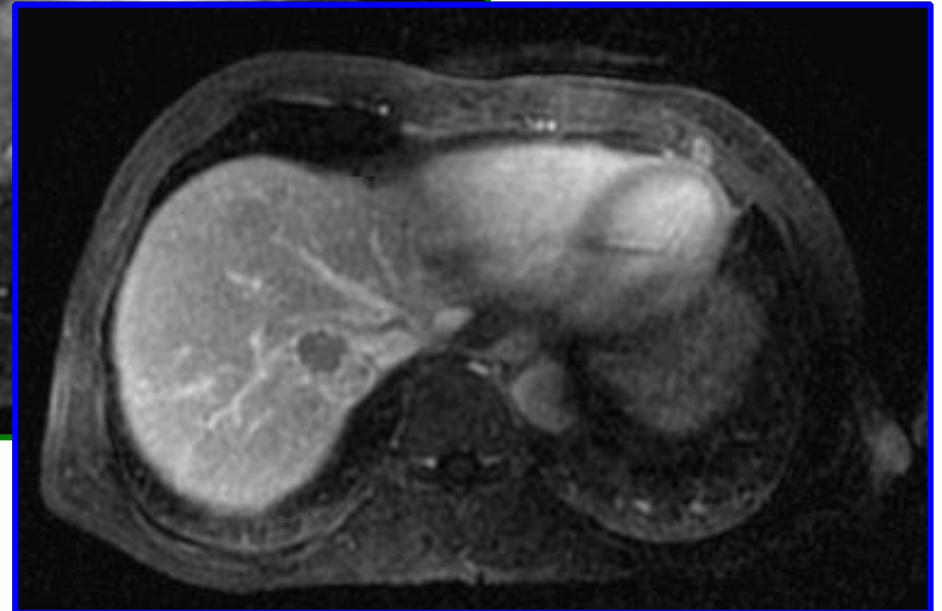
Non-Invasive Diagnosis: Arterial Enhancement, Venous Washout, Capsule and Threshold Growth



Arterial



Portal



Late venous phase

LIRADS System for HCC Diagnosis Schema

Lesion Characteristics		Arterial Phase Hypo- or Iso-Enhancement		Arterial Phase Hyper- Enhancement		
		< 20	≥ 20	< 10	10-19	≥ 20
Diameter (mm):		< 20	≥ 20	< 10	10-19	≥ 20
<ul style="list-style-type: none"> • “Washout” • “Capsule” • Threshold growth 	None:	LR-3	LR-3	LR-3	LR-3	LR-4
	One:	LR-3	LR-4	LR-4	LR-4 LR-5	LR-5
	≥ Two:	LR-4	LR-4	LR-4	LR-5	LR-5

Liver Biopsy in the Diagnosis of HCC

- Biopsy of small nodule within a cirrhotic liver seen on imaging studies may not be reliable.
- Sampling error occurs.
- Distinguishing HCC from dysplastic nodule is often erroneous.
- A “negative” biopsy can not rule out malignancy.
- Up to 30% of HCC patients can have a “non diagnostic” biopsy or tumor is inaccessible.

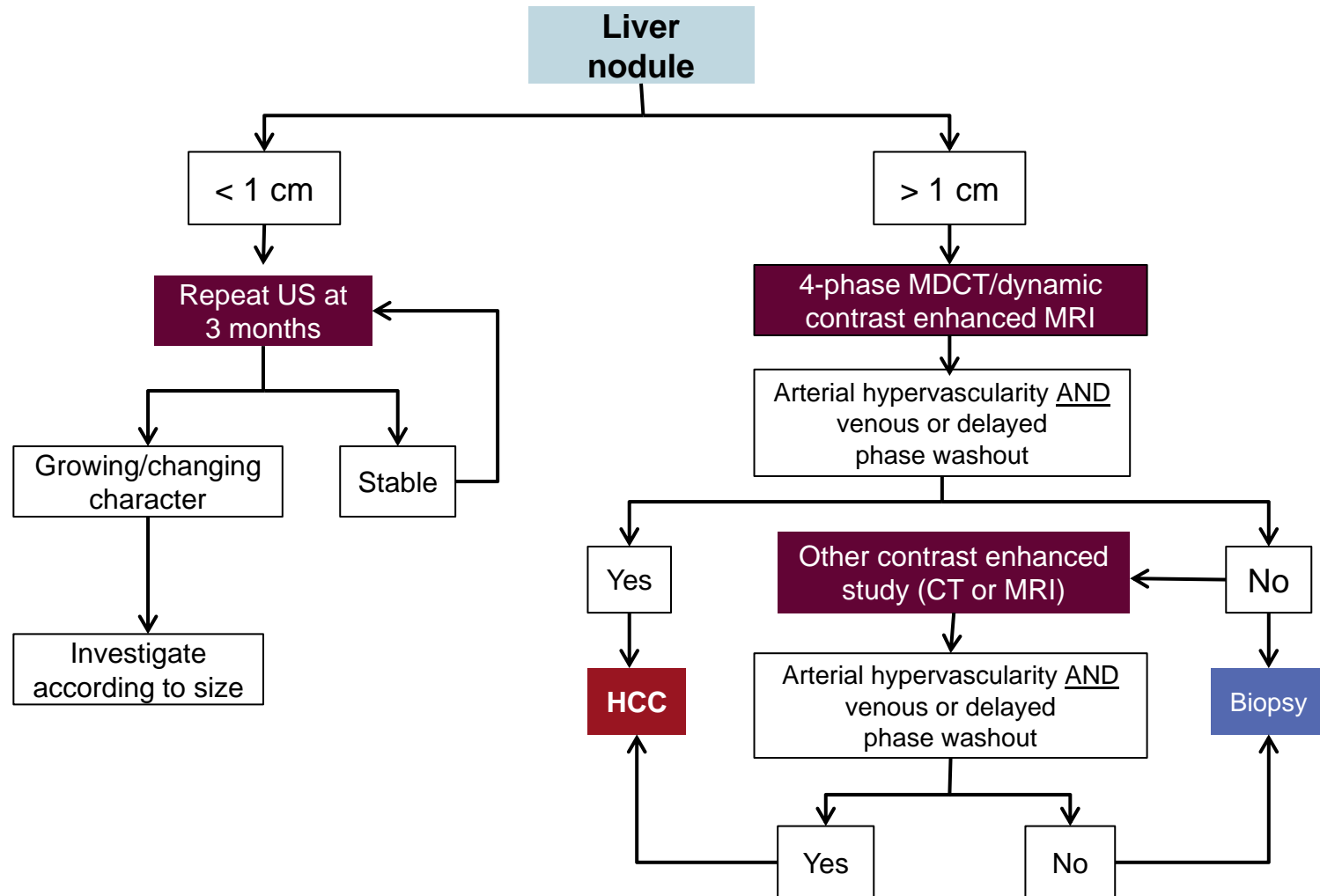
Diagnostic Values of HCC Biomarkers

Type of Test	Sensitivity (%)	Specificity (%)
AFP-L3	61.6	92
DCP	72.7	90
AFP	67.7	71
AFP-L3 + DCP	84.8	97.8
AFP-L3 + AFP	73.7	86.8
DCP + AFP	84.8	90.2

HCC Surveillance

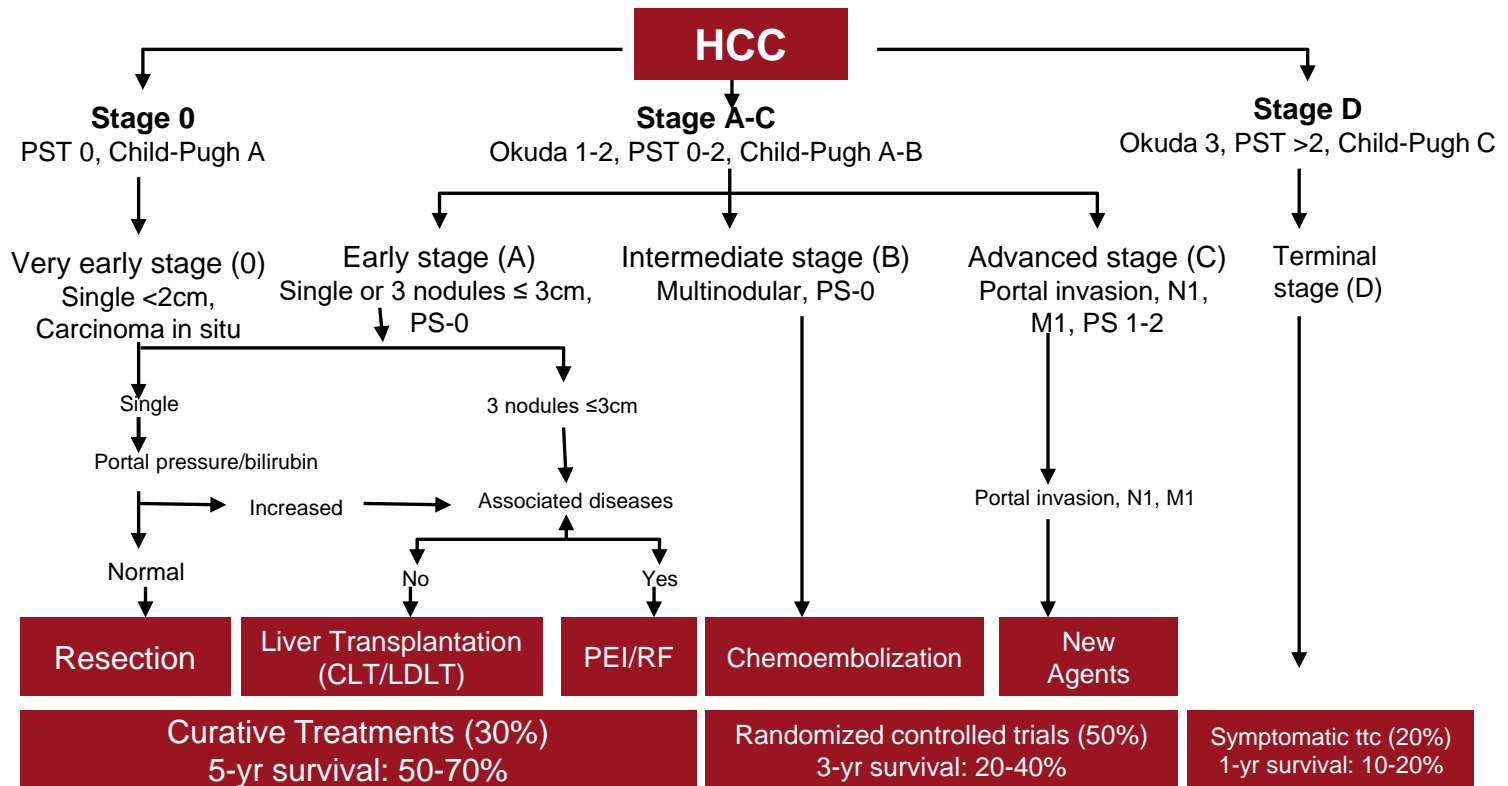
- Ultrasound with AFP improves sensitivity for tumor, and early tumor detection respectively in clinical practice.
- Ultrasound with AFP every 6 months appears to be the optimal surveillance strategy to maximize early HCC detection.
- MRI has higher sensitivity for detection of early tumor in patient with cirrhosis.

Diagnostic Algorithm for Hepatocellular Carcinoma (AASLD 2010 Practice Guidelines)



Barcelona Clinic Liver Cancer Staging System and Treatment Strategy for HCC

BCLC Staging and Treatment Schedule



Management Strategies for HCC

- Prevention:
 - Promote hepatitis B vaccination.
 - Treat chronic hepatitis B, C and other chronic liver disease.
 - Reduce the development of cirrhosis and progression to HCC.
- Early diagnosis
 - Surveillance for hepatocellular carcinoma in patients at risk by optimal screening tests.

HCC Treatment: A Multidisciplinary Approach

- By hepatologists, transplant and hepatobiliary surgeons, medical oncologists, interventional radiologists, and palliative care specialists.
- Curative therapy for HCC
 - Liver transplantation is the most effective treatment
 - Surgical resection for resectable disease in the absence of significant portal hypertension
 - Local ablation is as effective as surgical resection in very early or early stage

HCC Treatment: A Multidisciplinary Approach

- Trans-arterial chemo or radio-embolization
 - to downstage patients at intermediate/advanced stage
 - to prevent tumor progression while on the wait-list for OLT
- Sorafenib achieves modest prolongation of survival of patient with advanced stage HCC
- Future perspectives to improve clinical outcome of HCC
 - Immunotherapy
 - Targeted therapy

Summary

- Prevent HCC by hepatitis B immunization, and treatment of chronic liver diseases.
- Reduce the development of cirrhosis and progression to HCC.
- Diagnose early HCC in patients at risk by surveillance.
- Abdominal US with AFP every 6 months appears to be the optimal surveillance strategy to maximize early HCC detection.
- MRI has higher sensitivity for detection of early tumor in patient with cirrhosis.
- Improve the outcome of HCC by appropriate treatment through multidisciplinary approach.