Hepatocellular Carcinoma in HCV: Screening and Surveillance

Paulina Deming, PharmD, PhC
Associate Professor of Pharmacy-College of Pharmacy
Director- Viral Hepatitis Programs, Project ECHO
University of New Mexico Health Sciences Center

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For Patients with Cirrhosis

Baseline

- Baseline endoscopy of all patients with cirrhosis to screen for varices
- Avoid NSAID use (risk of bleed)

Every 6 months

- Surveillance for hepatocellular carcinoma (HCC)
- Ultrasound and AFP
- **Continued indefinitely… risk of liver cancer is 2-8% annually *even after HCV cure***

Liver Disease is a Progression of Increased Damage over Time

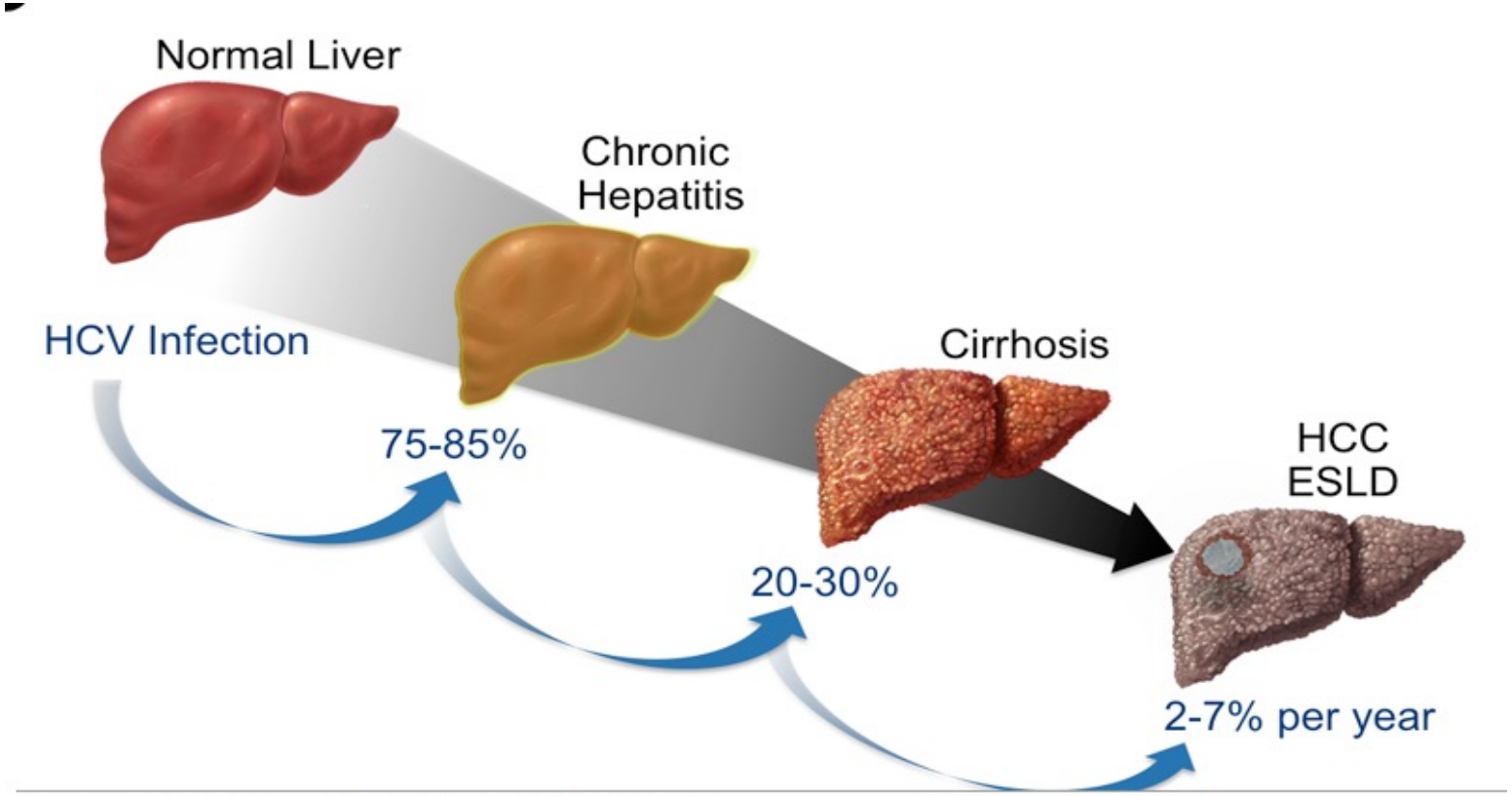
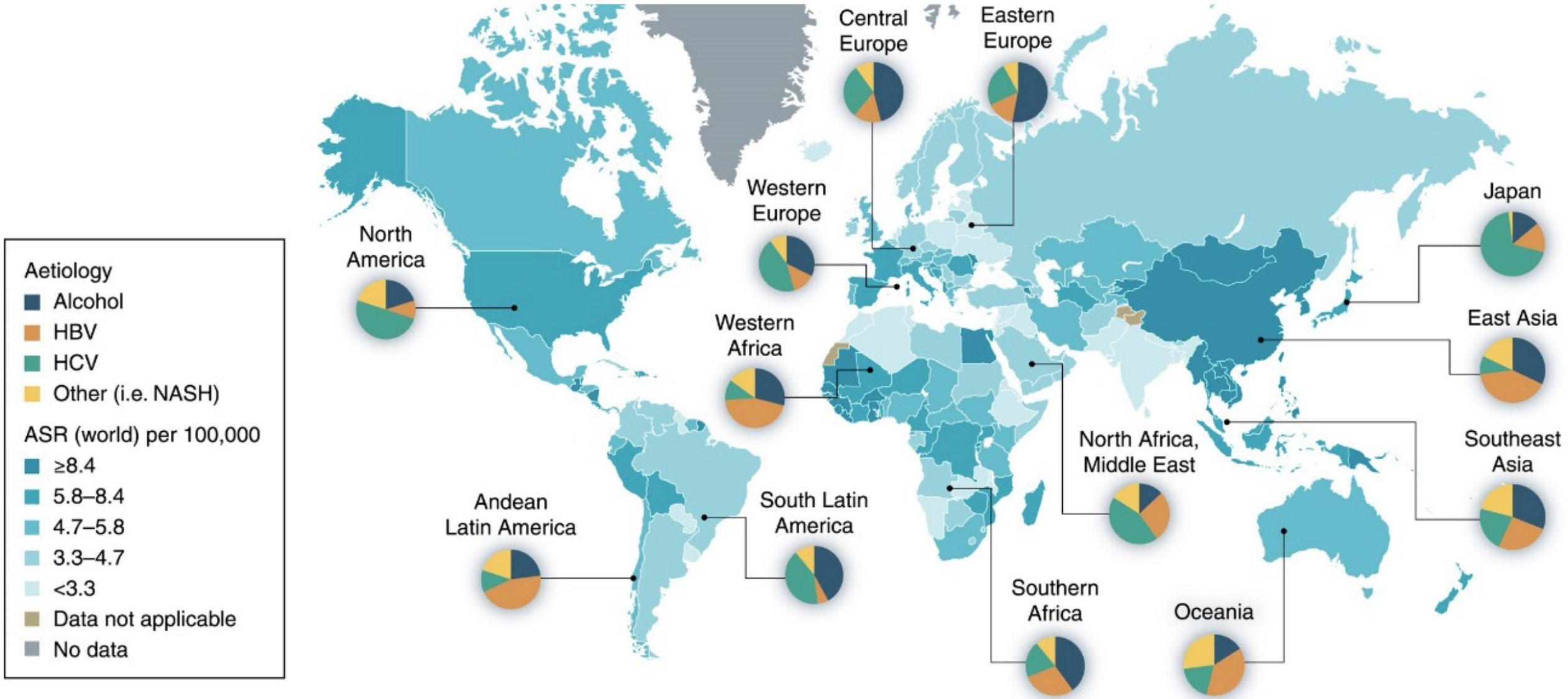


Figure 3 - Natural History Following Initial Infection with HCV
Following initial infection with HCV, approximately 75 to 85% of persons develop chronic infection. Among those with chronic infection, approximately 20 to 30% will eventually develop cirrhosis. Patients who have HCV-related cirrhosis have a 2 to 7% per year risk of developing either end-stage liver disease or hepatocellular carcinoma. Abbreviations: ESLD = end stage liver disease HCC = hepatocellular carcinoma

Cirrhosis is a spectrum of disease



Worldwide incidence of HCC and most common risk factors. ASR, age standardized incidence rate; HBV, hepatitis B virus; HCV, hepatitis C virus; NASH, nonalcoholic steatohepatitis; Reprinted with permission from Llovet et al. [9] and the International Agency for Research on Cancer/World Health Organization.

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HCC Prevention

Primary

- Hepatitis B vaccination
- Antiviral therapy for hepatitis B virus (HBV)
- Antiviral therapy for hepatitis C virus (HCV)
- Under investigation:
  - Coffee
  - Aspirin
  - Statins
  - Metformin

Secondary

- Detecting disease early and interventions to reduce disease impact
- Ultrasound and AFP for surveillance

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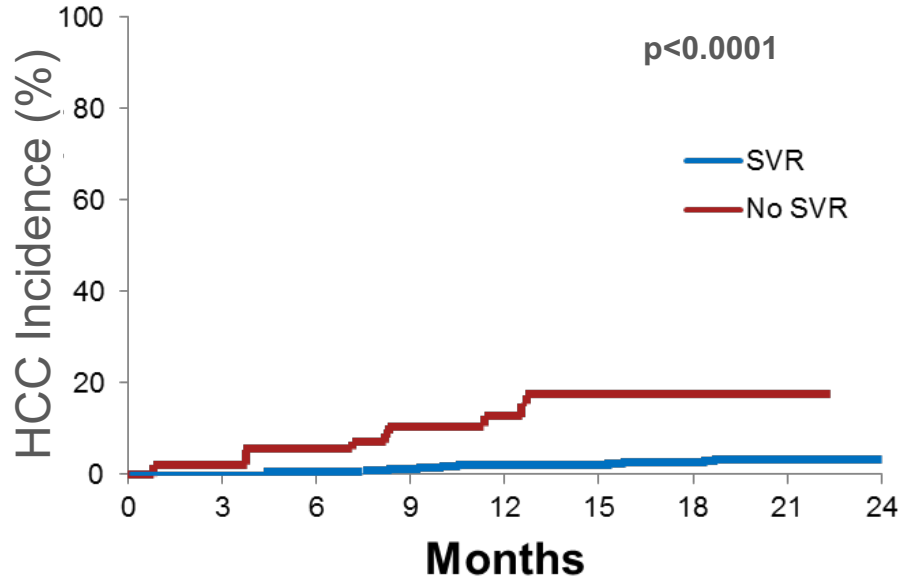
SVR as a Predictor of De Novo and Recurrent HCC in HCV Patients

Multicenter, prospective cohort of 1927 HCV-infected cirrhotic patients from Italy

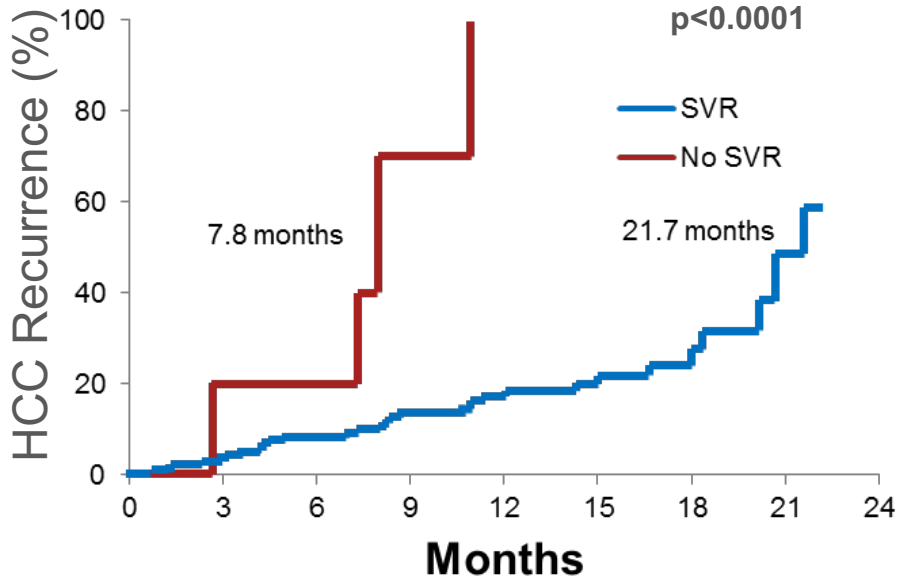
De Novo HCC

1766 patients no previous history of HCC; 50 patients developed HCC (50/1766 – 2.8%); Average annual incidence of 2.4%



HCC Recurrence

161 patients with previously treated HCC; 38 patients developed HCC; average annual incidence of 24.8%



SVR with DAA regimens is associated with a significant reduction of incidence and recurrence of HCC

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Lleo, EASL 2018, SAT-PS-154

Guidance Recommendations

- Vaccination against HBV
- Antiviral therapy for HBV and HCV
- Counseling to maintain healthy weight, balanced diet, avoiding tobacco and alcohol, and achieving adequate control of comorbid conditions including components of metabolic syndrome
- Consider recommending coffee

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Who Needs HCC Surveillance?

TABLE 1 - At-risk population for surveillance

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	

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What is Recommended for HCC Surveillance?

- US and AFP every 6 months
- Diagnostic contrast enhanced multiphasic MRI or CT if
  - Lesion on US 1 cm or greater OR
  - AFP $\geq$ 20 ng/mL OR
  - AFP increasing (doubling of AFP on two consecutive tests)

Interpreting Imaging Reports

CT/MRI Diagnostic Table

Arterial phase hyperenhancement (APHE)		No APHE		Nonrim APHE		
Observation size (mm)		< 20	≥ 20	< 10	10-19	≥ 20
Count additional major features: • Enhancing "capsule" • Nonperipheral "washout" • 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

LR-4 / LR-5

Observations in this cell are categorized based on one additional major feature:
- LR-4 – if enhancing "capsule"
- LR-5 – if nonperipheral "washout" **OR** threshold growth

Liver Reporting and Data System (LI-RADS) classification of computed tomography (CT) or magnetic resonance imaging (MRI) liver observations in patients who are at risk. LR, LI-RADS. Reprinted with permission from the American College of Radiology Committee on LI-RADS.[103]

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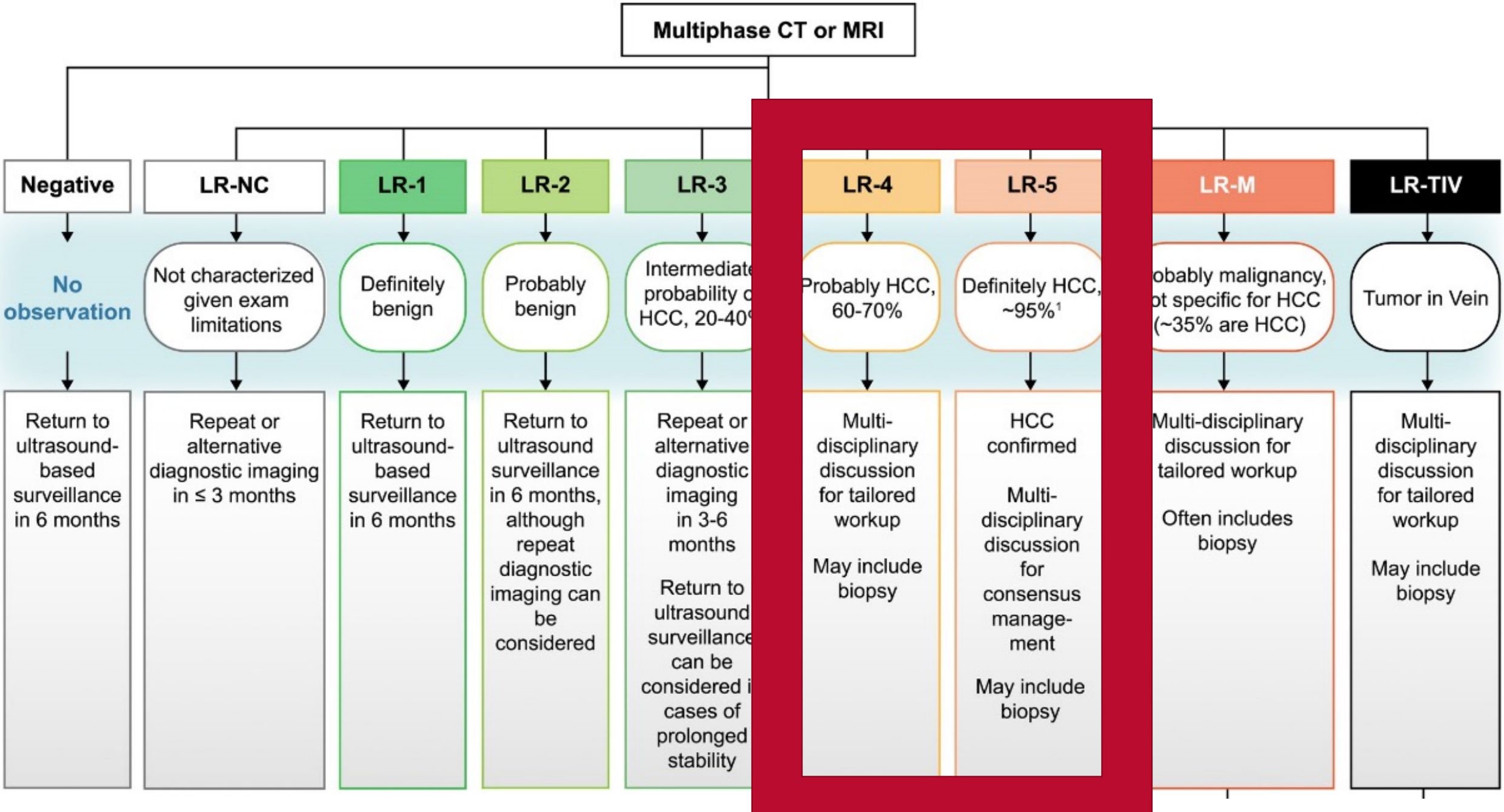
Multiphase CT or MRI
Negative
LR-NC
LR-1
LR-2
LR-3
LR-4
LR-5
LR-M
LR-TIV
No observation
Not characterized given exam limitations
Definitely benign
Probably benign
Intermediate probability of HCC, 20-40%
Probably HCC, 60-70%
Definitely HCC, ~95%[1]
Probably malignancy, not specific for HCC (~35% are HCC)
Tumor in Vein
Return to ultrasound-based surveillance in 6 months
Repeat or alternative diagnostic imaging in ≤ 3 months
Return to ultrasound-based surveillance in 6 months
Return to ultrasound surveillance in 6 months, although repeat diagnostic imaging can be considered
Repeat or alternative diagnostic imaging in 3-6 months
Return to ultrasound surveillance can be considered in cases of prolonged stability
Multi-disciplinary discussion for tailored workup
May include biopsy
HCC confirmed
Multi-disciplinary discussion for consensus manage-ment
May include biopsy
Multi-disciplinary discussion for tailored workup
Often includes biopsy
Multi-disciplinary discussion for tailored workup
May include biopsy

What About AFP?

- 40% of HCCs have normal AFP
- Elevated AFP can occur with other cancers- intrahepatic cholangiocarcinoma, gastric cancer, germ cell tumors
- Use of AFP plus ultrasound improves sensitivity for HCC

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Common Questions

Why is HCC surveillance recommended every 6 months?

- Associated with earlier tumor stage
- Associated with improved survival
- *Quarterly surveillance not found to improve survival as compared to semiannual*

Why use ultrasound?

- Concerns for radiation and contrast exposure with use of CT as surveillance
- Cost effectiveness, capacity, and patient acceptance concerns with MRI
- Elastography not effective for surveillance

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Why Continue HCC Surveillance?

Difference in Long-term Survival

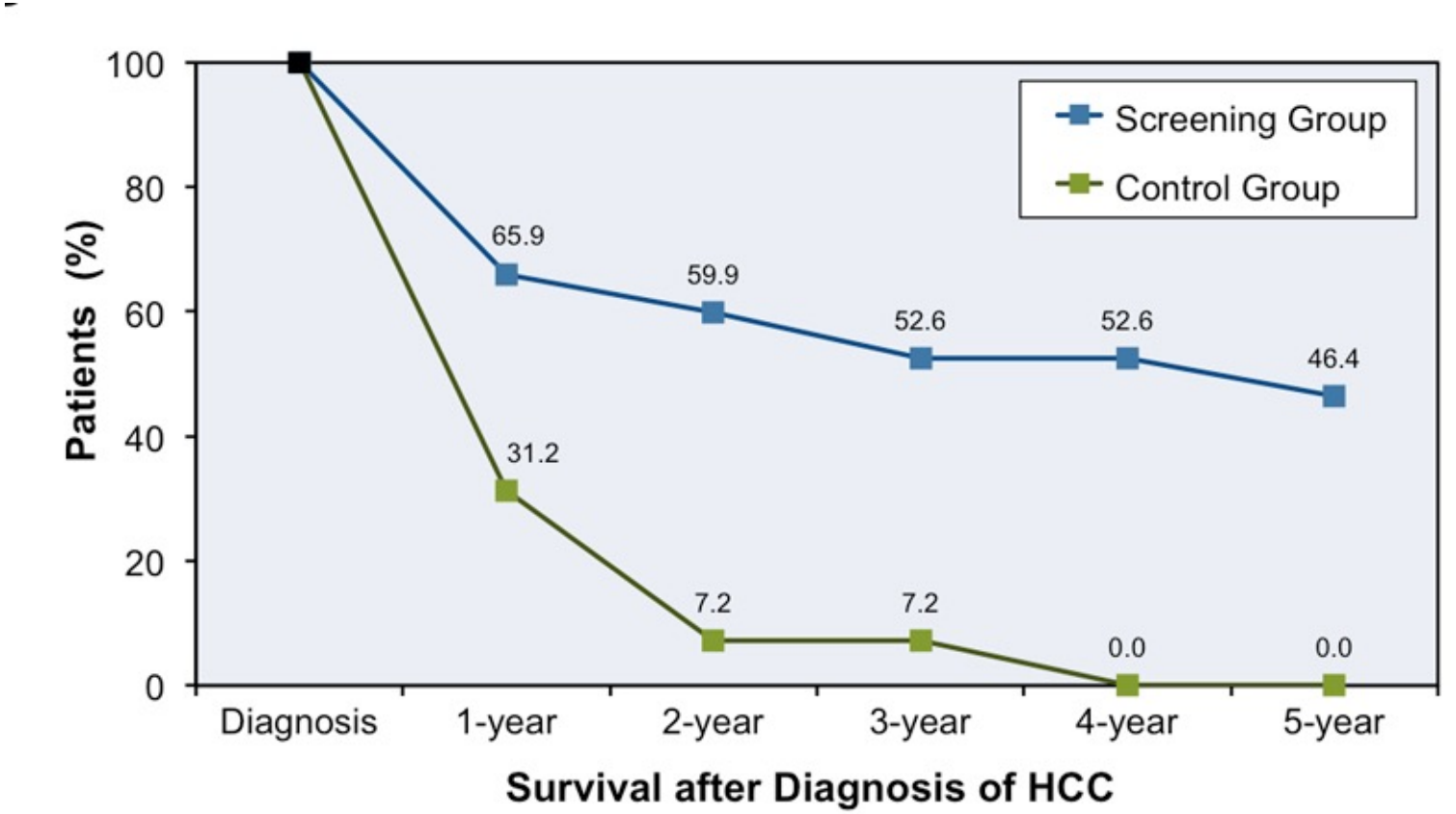

Figure 6 - Impact of Screening on Survival after Diagnosis of HCC
In this trial, patients with chronic viral hepatitis who underwent screening for HCC had improved survival after the diagnosis of HCC when compared with the control group that did not receive screening for HCC.

Source: Zhang BH, Yang BH, Tang ZY. Randomized controlled trial of screening for hepatocellular carcinoma. J Cancer Res Clin Oncol. 2004;130:417-22.

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