Hepatocellular Carcinoma Surveillance in Hepatitis B

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Who should be surveyed for HCC?

- HCC incidence among HBV patients without cirrhosis: 0.1 – 0.8 per 100 person-years
- HCC incidence among HBV patients with cirrhosis: 2.2 – 4.3 per 100 person-years
- E antigen persistence and high HBV DNA level increase risk of HCC
- Heavy smoking and alcohol use in HBV infection: increase HCC risk up to 9-fold

TABLE 1. PATIENTS AT THE HIGHEST RISK FOR HCC

Population Group	Threshold Incidence for Efficacy of Surveillance (>0.25 LYG; % per year)	Incidence of HCC
Surveillance benefit		
Asian male hepatitis B carriers over age 40	0.2	0.4%-0.6% per year
Asian female hepatitis B carriers over age 50	0.2	0.3%-0.6% per year
Hepatitis B carrier with family history of HCC	0.2	Incidence higher than without family history
African and/or North American blacks with hepatitis B	0.2	HCC occurs at a younger age
Hepatitis B carriers with cirrhosis	0.2-1.5	3%-8% per year
Hepatitis C cirrhosis	1.5	3%-5% per year
Stage 4 PBC	1.5	3%-5% per year
Genetic hemochromatosis and cirrhosis	1.5	Unknown, but probably >1.5% per year
Alpha-1 antitrypsin deficiency and cirrhosis	1.5	Unknown, but probably >1.5% per year
Other cirrhosis	1.5	Unknown
Surveillance benefit uncertain		
Hepatitis B carriers younger than 40 (males) or 50 (females)	0.2	<0.2% per year
Hepatitis C and stage 3 fibrosis	1.5	<1.5% per year
NAFLD without cirrhosis	1.5	<1.5% per year

Abbreviation: LYG, life-years gained.

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How do we survey for HCC in hepatitis B?

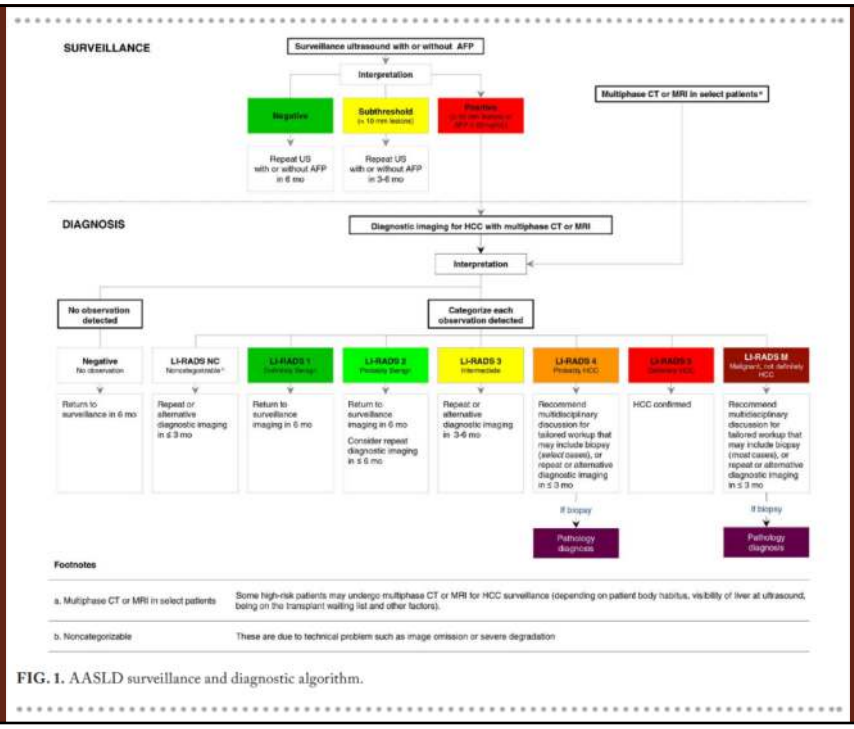

FIG. 1. AASLD surveillance and diagnostic algorithm.

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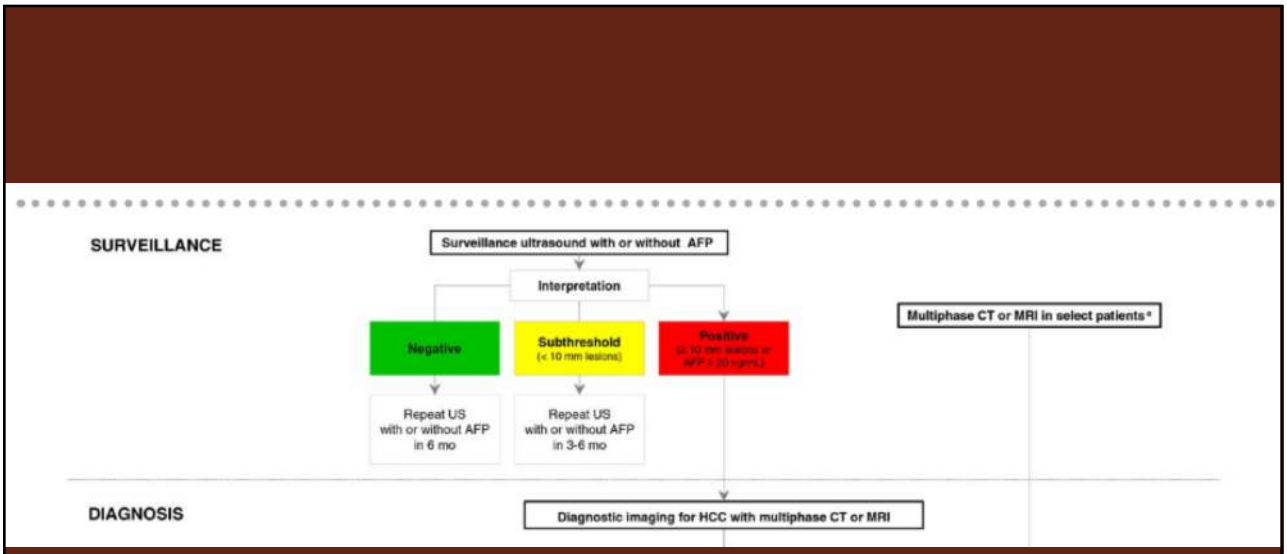

Hepatology, 2018

How do we survey for HCC in hepatitis B?

- US and AFP every 6 months
- US results may be variable; quality of study could be affected by multiple factors
- AFP >20 ng/mL is considered positive
  - Could be falsely positive
  - BUT longitudinal changes may be more sensitive
- Multiphasic CT and MRI: not enough data for screening, and not cost-effective

Does genotype play a role?

- Genotypes A-J
- Genotype A: Africa, Philippines, Japan, India, Brazil
- Genotypes B and C: most of Asia, Australia, Pacific Islands (?)
- Genotype D: Middle East, Mongolia, South Africa, Europe
- Genotype C: higher tendency of chronicity, positivity of e antigen, later e antigen seroconversion, HBV DNA level, worse clinical outcomes, and basal core promoter (BCP) mutations

How do mutations affect HCC development?

- Basal core promoter (BCP): modulates e antigen secretion
- Precore (PC): stop e antigen production
- E antigen: marker of HBV replication and infectivity
- Typically, loss of e antigen represents end of viral replication
- BCP and PC mutations allow HBV DNA to remain detectable in e antigen negative, e antibody positive patients
- BCP and PC mutations have been shown to increase risk of HCC development

How I approach HCC surveillance in HBV

- Ultrasound at time of diagnosis or at first visit with patient
- Use the guidelines as the minimum threshold for surveillance
- Positive family history of HCC: begin surveillance now
- Get genotype and mutations (if possible) to guide surveillance
- Genotype C: consider HCC surveillance earlier
- Be more aggressive with antiviral therapy
- Isolated HB core Ab: HCC surveillance is controversial, no guideline available, should be individualized consideration

References

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Mahalo!