Surveillance for Hepatocellular Carcinoma

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Disclosure Information

Dr Peters has reported the following financial relationships with commercial firms:

- Consultant: Merck & Co, Inc, Theravance, and Roche
- Data safety monitoring board: Biotron
- Scientific advisor: Clinical Care Options
- Her spouse is employed by Genentech (Roche)
Outline

① Indications for surveillance

② Surveillance methods

③ Evaluation of abnormal screening test
Indications for Surveillance
Who is at Risk for Hepatocellular Carcinoma (HCC)?

CHRONIC LIVER DISEASE

- Hepatitis C Virus
- Fatty Liver
- Alcohol
- Metabolic and Inherited
- Hepatitis B Virus

CIRRHOSIS

LIVER CANCER (HCC)
Surveillance Methods
Surveillance of HCC

- Surveillance: applying screening tests at regular intervals in patients at risk for HCC
- Most commonly used surveillance in clinical practice: ultrasound and alpha-fetoprotein (AFP) every 6 months
- The added value of AFP to ultrasound in surveillance has been questioned. AFP no longer included in 2011 American Association for the Study of Liver Disease (AASLD) guidelines; used in European Association for the Study of the Liver (EASL) and Asian Pacific Association for the Study of the Liver (APASL) guidelines

Bruix J and Sherman M - AASLD guidelines; Hepatology. 2011
Tumor Markers

- **AFP as a screening test**
  - 20%-40% with HCC have normal AFP
  - 20%-30% without HCC have abnormal AFP
  - The higher the AFP, the more likely the diagnosis of HCC

- **Des-gamma-carboxy prothrombin (DCP; aka PIVKA-II)** not better than AFP

- **AFP as a prognostic marker**
  - Predicts overall mortality in HCC
  - Predicts prognosis after resection
  - Predicts prognosis after liver transplant

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HCC Monitoring Guidelines for HCV Patients

- All patients with cirrhosis even after SVR
- Screening strategy
  - Ultrasonography at intervals of 6 or 12
  - Serum AFP testing: no longer recommended by AASLD guidelines
- Based on
  - Low incidence of HCC in those at risk: 1%-4% per year
  - Slow growth of these tumors, mean estimated doubling time of 136 days
Recognize Advanced Liver Disease

- Diagnose cirrhosis
  - Liver biopsy
  - Noninvasive markers/ transient elastography
  - Ultrasound low sensitivity 55%-70%, accuracy 77%-87%
    - Better if portal hypertension
- Clinical evidence of portal hypertension
  - Low platelets
  - Low white cell count
  - Splenomegaly
  - Spider nevi
Evaluation of Abnormal Screening Test
Diagnostic Criteria for HCC
AASLD Guidelines (Modified)

- Tumor > 1 cm - One imaging (multi-phase CT/MRI) showing typical HCC characteristics*

* Arterial phase hypervascularity and delayed phase “washout”

- Liver biopsy is not necessary for confirming diagnosis, but recommended if imaging criteria not met

Bruix J and Sherman M. AASLD guidelines; Hepatology. 2011
Biopsy is not necessary to confirm HCC diagnosis if the lesion meets radiologic criteria in the appropriate clinical setting.

*False negative biopsy common in clinical practice and may need to delay in diagnosis and treatment*

*Tumor seeding along the biopsy tract in 1%-5%*

Biopsy is necessary in selected cases if atypical radiologic appearance or lack of strong risk factor for HCC.
Barcelona Clinic Liver Cancer (BCLC) Staging Classification

HCC

Stage 0
PST 0, Child-Pugh A

Stage A-C
Okuda 1-2, PST 0-2, Child-Pugh A-B

Stage D
Okuda 3, PST >2, Child-Pugh C

Very early stage (0)
single < 2 cm, CA in situ

Early stage (A)
single or 3 nodules < 3 cm, PS 0

Intermediate stage (B)
multinodular, PS 0

Advanced stage (C)
portal vein invasion, N1,M1, PS 1-2

Terminal stage (D)

5-yr survival: 50%-70%

3-yr survival: 20%-40%

Symptomatic Tx
1-yr survival: 10%-20%

Resection
Liver Transplantation
PEI/ RFA
TACE
New agents

Increased
Associated diseases

3 nodules ≤ 3cm

No
Normal

Increased
Normal

Yes

Portal pressure/ bilirubin

Adapted from Llovet JM et al. Lancet 2003
Surgical Treatment for HCV Cirrhosis and Liver Function

NON-CIRRHOTIC → RESECTION
5% in Western countries
40% in Asia

CIRRHOTIC

Child A
Child B
Child C → TRANSPLANT
Hepatic Resection for HCC with Cirrhosis

“Ideal” candidate

- Good liver function: Child-Pugh class A cirrhosis
- No portal hypertension (suggested by varices, enlarged spleen, platelets < 100,000/µL)
- Normal bilirubin
- Single lesion ≤ 5 cm
- Location of tumor in left lobe
Liver Transplantation for HCC
Milan Criteria

1 lesion ≤ 5 cm

2 to 3, none > 3 cm

Absence of macroscopic vascular invasion
Absence of extrahepatic spread

Local Regional Therapies for HCC

CHEMOEMBOLIZATION
Conventional and drug-eluting beads

ABLATIONS

CHEMICAL
Percutaneous ethanol injection (PEI)

THERMAL
Radiofrequency ablation (RFA)
  (Laparoscopic, percutaneous or open)

Microwave/ Cryoablation

RADIOEMBOLIZATION (YITTRIUM - 90)
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- Based on
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Summary

- All patients with cirrhosis require monitoring
- Ultrasound first line
  - AFP of limited value in diagnosis
  - CT or MRI if lesion found
- There are many treatment modalities available depending upon size and number of lesions
End

This presentation is brought to you by the International Antiviral Society-USA (IAS-USA) in collaboration with Hepatitis Web Study & the Hepatitis C Online Course

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