Hepatocellular Carcinoma (HCC)

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Worldwide Incidence of Hepatocellular Carcinoma

High (> 30:100,000)
Low or data unavailable (< 3:100,000)
Intermediate (3-30:100,000)

El-Serag HB, Gastroenterology 2004
## Association Between Time Period of HCC Diagnosis (1996-1999 vs. 1993-1996) and Presence of Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Adjusted Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV</td>
<td>2.26 (1.79-2.86)</td>
</tr>
<tr>
<td>HBV</td>
<td>1.67 (1.22-2.28)</td>
</tr>
<tr>
<td>Alcohol-related liver disease</td>
<td>1.16 (0.95-1.42)</td>
</tr>
<tr>
<td>Non-specific cirrhosis</td>
<td>0.84 (0.68-1.03)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>0.83 (0.70-0.98)</td>
</tr>
</tbody>
</table>

*Davila JA, et al, Gastroenterology 2004*
Why is HCC Incidence Rising?

Increasing prevalence of patients with cirrhosis

- Rising incidence of cirrhosis
  - HCV (main reason)
  - HBV
  - Other (?NAFLD/insulin resistance)
- Improved survival of patients with cirrhosis

El-Serag HB, Gastroenterology 2004
HCC Epidemiology

Risk Factors for HCC

- Cirrhosis from any cause
  - HCV
  - HBV
  - Heavy alcohol consumption
  - Non-alcoholic fatty liver disease
- HBV
- Inherited metabolic diseases
  - Hemochromatosis
  - Alpha-1 antitrypsin deficiency
  - Glycogen storage disease
  - Porphyria cutanea tarda
  - Tyrosinemia
  - Autoimmune hepatitis
HCC Epidemiology

HCV Cirrhosis and Hepatoma

Arterial phase

Equilibrium

HCC
HCC Epidemiology

HCV Cirrhosis and HCC

Multiple small foci of HCC
Risk Factors for HCC Among US Veterans

N = 823 cases with HCC
N = 3,495 controls

El-Serag HB, & Everhart JE, Am J Gastro 2001
Prevention of HCC in HCV

• Will sustained viral remission decrease the risk for HCC?

• Will long term interferon therapy slow progression to/of cirrhosis?

• Will long term interferon therapy prevent HCC?
Metabolic Syndrome (Syndrome X)

• Estimated to affect 47 million Americans

• Diagnosis based on 3 or more of the following:
  • Abdominal obesity (waist > 40” for men and 34.5” for women)
  • Triglyceride level >150 mg/dL
  • HDL <40 mg/dL for men and <50 mg/dL for women
  • Fasting blood glucose ≥110 mg/dL
  • Blood pressure ≥130/85
# Clinical Features at Presentation

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Percent of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>23%</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>32%</td>
</tr>
<tr>
<td>Ascites</td>
<td>8%</td>
</tr>
<tr>
<td>Jaundice</td>
<td>8%</td>
</tr>
<tr>
<td>Anorexia/weight loss</td>
<td>10%</td>
</tr>
<tr>
<td>Malaise</td>
<td>6%</td>
</tr>
<tr>
<td>Bleeding</td>
<td>4%</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>2%</td>
</tr>
</tbody>
</table>
HCC Diagnosis

Triple Phase Imaging of Hepatocellular Carcinoma

- Pre-contrast
- Arterial Phase
- Portal Venous Phase
- 5-min Delayed
Progression Towards HCC

HCC Pathology

Chronic Liver Disease
Cirrhosis
HCC

Thorgiesson S, et al, Nat Genet 2002
Key Concepts in the Management of Hepatocellular Cancer

- Liver transplantation achieves the best outcome in HCC patients with decompensated cirrhosis who meet criteria.
- Surgical resection is most effective for non-cirrhotic patients or those with cirrhosis and preserved liver function and can be followed by salvage OLT.
- Patients with small tumors are best stratified for resection or OLT by the presence of clinically-significant portal hypertension and/or increased serum bilirubin.
- Local ablative methods are an option for small solitary nodules and those who are not surgical candidates.
- Transarterial chemoembolization improves survival in intermediate-advanced HCC.
**Cancer of the Liver Italian Program (CLIP) Staging System**

- **Child-Pugh stage**
  - A: 0
  - B: 1
  - C: 2

- **Tumor morphology**
  - Uninodular and extent ≤ 50% of liver: 0
  - Multinodular and extent ≤ 50% of liver: 1
  - Massive or extent ≥ 50% of liver: 2

- **Alpha fetoprotein (ng/dl)**
  - < 400: 0
  - ≥ 400: 1

- **Portal vein thrombosis**
  - No: 0
  - Yes: 1

_The CLIP Investigators, Hepatology 1998_
Ablation Therapy

- Chemically-mediated ablation
  - Ethanol injection
  - Acetic acid injection
- Energy-mediated ablation
  - Cryoablation
  - Microwave ablation
  - Radiofrequency ablation

HCC Treatment
Radiofrequency Ablation for Hepatocellular Carcinoma

Probe insertion

Deployment of tines and treatment of tumor and surrounding region
Planning Angiogram for Y90 Microsphere Treatment

- Evaluate hepatic arterial anatomy
- Occlude any branches supplying extrahepatic structures
- Infuse Tc-99m-macroaggregated albumin
  - confirm perfusion limited to the liver
  - measure the lung shunt (<16.5 mCi Y-90 to the lungs)
Management Algorithm for HCC

No Cirrhosis

- No extrahepatic spread
- No involvement of major portal structures
- Tumor may be large

Surgical Resection

- Extrahepatic spread
- Involvement of major portal structures
- Multilobar disease

Local Chemo- or Radio-embolization, Systemic Chemotherapy, or Targeted Therapy Trials
Management of HCC in Patients with Cirrhosis

- **Child class A**
  - No Portal Hypertension
  - Normal Bilirubin

### Early Disease
- One \( \leq 5 \) cm tumor
- 2 or 3 \( \leq 3 \) cm tumors
- No extrahepatic spread

### Intermediate Disease
- Large tumor
- Multiple nodules
- No extrahepatic spread

### Advanced Disease
- Massive tumor
- Multiple nodules
- Extrahepatic spread

#### Resectable?
- Yes
  - **Surgical Resection**
  - **Orthotopic Liver Transplantation**
  - **Ablation** (RF or EtOH)
    - \( \leq 3 \) tumors
    - \( \leq 4 \) cm

- No
  - **Salvage**
  - **Transplant Candidate?**
    - Yes
      - **Systemic Chemotherapy or Targeted Therapy** (Chemoembolization, Radioembolization "TheraSphere")
    - No
      - **Local Chemo- or Radiotherapy**

#### Biopsy

- **No Biopsy**