HEPATOCELLULAR CARCINOMA: SCREENING, DIAGNOSIS, AND TREATMENT
INTRODUCTION:

- **Hepatocellular carcinoma (HCC):**
  - Fifth most common cancer worldwide
  - Third most common cause of cancer mortality
  - In Egypt: 2.3% of all cancers
  - About 90% of all HCC is unique in that it develops in the background of well-recognized risk factors with increase in incidence in resource-rich countries
  - Further rise in incidence is predicted in the next decades due to the accumulation of patients with chronic liver diseases who are expected to develop HCC
Risk factors

• HBV
• HCV
• Alcohol
• Aflatoxin

Emerging risk Factors

• Nonalcoholic Fatty Liver Disease
• Obesity
• Diabetes Mellitus
• Tobacco
• Oral Contraceptives
• Hemochromatosis
• Genetic Epidemiology
## Introduction

A map of the world highlights different regions and their respective risk factors. The map uses color codes to indicate the severity of each risk factor. The color legend is as follows: green for risk factors below 3.3, yellow for 3.3–5.6, orange for 5.6–10, red for 10–15, and dark red for 15–99.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Europe/United States</th>
<th>Japan</th>
<th>Africa/Asia</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>22 (4–58)</td>
<td>20 (18–44)</td>
<td>60 (40–90)</td>
</tr>
<tr>
<td>HCV</td>
<td>60 (12–72)</td>
<td>63 (48–94)</td>
<td>20 (9–56)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>45 (8–57)</td>
<td>20 (15–33)</td>
<td>(11–41)</td>
</tr>
<tr>
<td>Tobacco</td>
<td>12 (0–14)</td>
<td>40 (9–51)</td>
<td>22</td>
</tr>
<tr>
<td>Aflatoxin exposure</td>
<td>Limited</td>
<td>Limited</td>
<td>High</td>
</tr>
<tr>
<td>Other</td>
<td>&lt;5</td>
<td>–</td>
<td>&lt;5</td>
</tr>
</tbody>
</table>
HCC is one of the fastest rising cancers in middle age men.

Incidence Rate per 100,000

Year of Diagnosis

45 - 49 Years
50 - 54 Years

El-Serag HB et al, Ann Intern Med 2003
WHY IS THE INCIDENCE RISING?

Increasing prevalence of patients with cirrhosis

- Rising incidence of cirrhosis
  - HCV (main reason)
  - HBV
  - Other
- Improved survival of patients with cirrhosis

*El-Serag HB, Gastroenterology 2004*
HCV Infection

Chronic Hepatitis

Cirrhosis

HCC

1% (1%-3%/year)

15% (10%-30%)

90% (60%-95%)

100

25 years

Goodgame B, et al., Am J Gastroenterol 2003
HCC AFTER IFN THERAPY FOR HCV

Cumulative Incidence of HCC (%)

Follow-up (yr)

0 1 2 3 4 5 6 7

No Response
Relapse
Sustained Response

CLINICAL OUTCOME OF CHRONIC HEPATITIS B

Chronic HBV Infection

Inactive Carrier State

Chronic Hepatitis

Cirrhosis

HCC
HBV DNA Associated with Increased Risk of HCC

- Likelihood of HCC in individuals with detectable HBV DNA is 3.9 times more than those with undetectable HBV DNA
- Risk associated with increasing HBV DNA levels
- These data support possibility of preventing long-term risk of HCC by inducing sustained suppression of HBV replication

PRIMARY PREVENTION OF HCC

• Vaccinate to HBV!
• Treat HCV with interferon
• Treat HBV
• Abstain from alcohol
• Phlebotomize if pt has iron overload
• Weight loss
Surveillance Recommendations

• The target population for surveillance are those with liver cirrhosis (and HBV-infected patients)

• AFP and US are the recommended screening tests for HCC in patients at the highest risk

• Based on tumor doubling time and studies, the recommended interval for surveillance is every 6 months in patients with cirrhosis

• Screening increases likelihood of HCC diagnosis
  • Small and potentially treatable
  • May reduce mortality
SURVEILLANCE FOR HCC PROLONGS SURVIVAL


Survival Probability (%)

Time (Months)

All HCC Patients = 451

Screened

Not screened

P < 0.001

(214)
(123)
(208)
(110)

(66)
(37)

(58)
(22)

(66)
(19)

(37)

(22)

(14)

(110)

(123)

(208)

(214)

P < 0.001
Cost-Effectiveness of HCC Surveillance

- Surveillance with bi-annual alpha-fetoprotein (AFP) and ultrasonography in Child class A cirrhotics had cost-effectiveness ratios between $26,000 and $55,000 per QALY

- 2 other studies show cost-benefits of HCC surveillance

Lin OS, et al, Aliment Pharmacol Ther 2004
Cirrhosis or HBV

US + AFP q6 mo

Lesion

<1 cm
- Reimage 3 mon

1-2 cm
- Biopsy vs Reimage 3 months
- AFP-L3, DCP Quad phase CT MRI

>2 cm
- HCC Diagnosed

No Lesion

Increased AFP

Normal AFP

Continue q6 mo surveillance
QUAD PHASE IMAGING OF HEPATOCELLULAR CARCINOMA

HCC Diagnosis
LIVER FUNCTION ASSESSMENT:

| Modified Child-Pugh Classification for Assessing Degree of Liver Impairment |
|---|---|---|---|
| Criterion     | 1 Point | 2 Points | 3 Points |
| Bilirubin     | \( \leq 2 \) | 2–3      | >3       |
| Albumin       | >3.5     | 2.8–3.5  | <2.8     |
| INR           | <1.7     | 1.7–2.2  | >2.2     |
| Ascites       | None     | Mild     | Moderate |
| Encephalopathy| None     | Mild     | Moderate |

INR, international normalized ratio.

Adding the points for each patient’s factors determines the Child-Pugh “class” as follows: A = 5–6 points, B = 7–9 points, C = 10–15 points.
Factors Determining Prognosis of Hepatocellular Cancer

- Tumor stage
  - Size
  - Number
  - Location

- Vascular invasion
- Extrahepatic spread

- Liver function

- Overall patient health
  - Performance status, Karnofsky score

- Intervention-specific outcome
Management of Hepatocellular Carcinoma

• Most algorithms distinguish between
  • Early HCC - Curative intent possible
  • Intermediate-Advanced HCC - Curative intent not possible, but not terminal
  • Advanced/Terminal HCC - Palliative options only
TREATMENT FOR HCC

- Resection
- Transplantation

- Image-guided interventions
  - PEI
  - RFA
  - Chemoembolization

Newer modalities

60 – 70%
5yr survival

40 – 50%
5yr survival