Liver Cancer: Epidemiology and Health Disparities

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Onyx Pharmaceuticals
Epidemiology
Primary Liver Cancer

- Hepatocellular cancer (HCC) accounts for 70%–85% of primary liver malignancies worldwide\(^3\)
- More common in men than women (> 2:1 ratio)\(^1\)

**Incidence**

- Fifth leading cause of cancer in men and eighth leading cause of cancer in women globally: \(\approx 560,000\) new annual cases\(^1\)
- \(\approx 28,720^*\) (21,370 in men and 7,350 in women) new cases in United States in 2012\(^2\)

**Mortality**

- Third leading cause of cancer-related death globally\(^3\)
- Fifth leading cause of cancer-related death in men and ninth in women in United States\(^2\)

*Estimated; includes intrahepatic bile duct cancers.

2. American Cancer Society: Cancer Facts & Figures 2013. Atlanta, GA.
Epidemiology
Primary Liver Cancer

- In the past 30 years the incidence and mortality rates for HCC in the United States have more than doubled\(^1\)
  - Rising rates of Hepatitis C viral infection (HCV)
  - Migration from Hepatitis B (HBV) endemic areas
  - Rising rates of obesity in the United States which is the leading cause of NAFLD and NASH

\(^1\)El-Serag HB et al, Ann Intern Med 2003
HCC Epidemiology

Worldwide Incidence of Hepatocellular Carcinoma

El-Serag HB,
Gastroenterology
2004

- High (> 30:100,000)
- Intermediate (3-30:100,000)
- Low or data unavailable (< 3:100,000)
Global Variation in Primary Liver Cancer Incidence

- Eastern Asia
- South-Eastern Asia
- Middle Africa
- Western Africa
- Southern Africa
- Melanesia
- Southern Europe
- Micronesia/Polynesia
- Northern Africa
- Central America
- Western Europe
- Eastern Africa
- North America
- Caribbean
- South America
- Australia/New Zealand
- Central & Eastern Europe
- Western Asia
- Northern Europe
- South-Central Asia

Regional Variations in HCC-related Mortality

Mortality Rate / 100,000 Age-Adjusted

El-Serag HB, Gastroenterology 2004
HCC Epidemiology

Incidence, United States

Incidence\(^1\*\)

- Median age at diagnosis
  - 64 years\(^2\)
- Highest mean annual % change in incidence rate in persons 50-59 years\(^2\)
- Increasing incidence of HCC likely caused by\(^3\)
  - Aging of persons who acquired HCV during 1960s
  - Improved survival of cirrhotic patients
  - Increasing obesity and diabetes rates

Deaths\(^1*\)

- 9th leading cause of cancer deaths
- 5th leading cause of cancer deaths

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>21,370</td>
<td>7,350</td>
<td>13,980</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Deaths</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>6,570</td>
<td>13,980</td>
<td>7,350</td>
</tr>
</tbody>
</table>

*Estimated; includes intrahepatic bile duct cancers.

Epidemiology

HCC risk factors

- Nonalcoholic Steatohepatitis
- Alcohol
- Autoimmune factors
- Inherited factors
- Hepatitis C
- Hepatitis B
- Aflatoxin B1

Racial Incidence Rates For HCC In The United States

HCC Epidemiology

Age-adjusted incidence rate per 100,000

El-Serag HB et al, Ann Intern Med 2003
HCC Epidemiology

Incidence of HCC in Whites (Hispanics and non-Hispanics)

Age-adjusted incidence rate per 100,000

Year

1993 1995 1997 1999 2001 2003
Racial Distribution of detected HCC in the United States

HCV-Related HCC and Ethnicity in the US

- Ethnicity of patients with HCC and serological testing for HBsAg and anti-HCV, in absolute numbers

### Ethnicity of Patients with HCC

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Number (n)</th>
<th>HBsAg</th>
<th>Anti-HCV</th>
<th>Both markers</th>
<th>Neither</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>410</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>107</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>95</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Future Trends in HCC Incidence

Distribution of risk factors among HCC cases
- HCV 24% to 60%
- NASH/NAFLD 13% up to 50%

Prevalence of risk factors in the general population
- HCV 2%
- Obesity 30%, overweight 60%
- HBV 0.4%
Rate of Chronic HCV Infection in the US
Highest Among Young African-American Adults

% Anti-HCV Positive

African-American
Hispanic
Caucasian

Age Group (years)
6-11 12-19 20-29 30-39 40-49 50-59 60-69 >70

CDC, MMWR 1998
The Estimated Annual Percentage Change (EAPC) in Hepatocellular Carcinoma Incidence by Race/Ethnicity and Sex During the 1992-2002 EAPC (95% Confidence Interval)

<table>
<thead>
<tr>
<th>Race Ethnicity</th>
<th>EAPC (95%) Confidence interval (n=14,210)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic</td>
<td></td>
</tr>
<tr>
<td>• Male</td>
<td>4.7 (2.8-6.6)</td>
</tr>
<tr>
<td>• Female</td>
<td>3.5 (1.4 to 5.8)</td>
</tr>
<tr>
<td></td>
<td>6.8 (3.6 to 10.1)</td>
</tr>
<tr>
<td>White non-Hispanic</td>
<td></td>
</tr>
<tr>
<td>• Male</td>
<td>4.3 (2.9 to 5.8)</td>
</tr>
<tr>
<td>• Female</td>
<td>4.0 (2.4 to 5.6)</td>
</tr>
<tr>
<td></td>
<td>3.6 (1.9 to 5.3)</td>
</tr>
<tr>
<td>Black</td>
<td></td>
</tr>
<tr>
<td>• Male</td>
<td>4.3 (2.7 to 6.0)</td>
</tr>
<tr>
<td>• Female</td>
<td>5.4 (3.5 to 7.2)</td>
</tr>
<tr>
<td></td>
<td>1.7 (-2.1 to 5.8)</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td></td>
</tr>
<tr>
<td>• Male</td>
<td>0.6 (-0.8 to 2.0)</td>
</tr>
<tr>
<td>• Female</td>
<td>0.7 (-0.8 to 202)</td>
</tr>
<tr>
<td></td>
<td>0.7 (-1.2 to 2.8)</td>
</tr>
</tbody>
</table>
## HCC Epidemiology

**Effect of treatment on survival**

Most Patients Have Advanced Disease at Diagnosis\(^1\)

<table>
<thead>
<tr>
<th>Disease Stage and Treatment Status</th>
<th>1-Year Survival(^a) (%)</th>
<th>Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Localized</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated</td>
<td>83</td>
<td>Liver Transplantation, Liver Resection, RFA</td>
</tr>
<tr>
<td>Not Treated</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td><strong>Regional</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated</td>
<td>60</td>
<td>Locally ablative or regional therapy to tumor</td>
</tr>
<tr>
<td>Not Treated</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td><strong>Distant</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated</td>
<td>30</td>
<td>Systemic treatment, clinical trials or palliative therapy</td>
</tr>
<tr>
<td>Not Treated</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)2003-2004, diagnosis years.

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Outcomes:
Dependent on treatment eligibility at time of diagnosis

- Early diagnosis is better for HCC
- 5 year survival for untreated HCC is 6-7%  
  - Improvement in survival have not been uniform, there are racial/minority and insurance related disparities
  
- 4-year survival is 74% for patients who diagnosed early enough for liver transplantation

2 El-Serag HB et al., Hepatology. 2001;33:62-65
Survival by treatment of liver cancer in patients who had non-metastatic disease (data from 1998-2004, N=8392)

Metastatic Liver Cancer
(survival by race/ethnicity 1973-2004, n=17,209)

Artinyan A et al., Cancer, March 2010, 1367-1377
Rate of Intervention by Race/Ethnicity for Patients who had non-metastatic disease

<table>
<thead>
<tr>
<th>Treatment</th>
<th>White</th>
<th>Asian/PI</th>
<th>Hispanic</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td>No surgery</td>
<td>2563 (62%)</td>
<td>1048 (55%)</td>
<td>837 (67%)</td>
<td>672 (69%)</td>
</tr>
<tr>
<td>Ablation</td>
<td>396 (10%)</td>
<td>232 (12%)</td>
<td>109 (9%)</td>
<td>93 (10%)</td>
</tr>
<tr>
<td>Resection</td>
<td>691 (17%)</td>
<td>469 (25%)</td>
<td>138 (11%)</td>
<td>145 (15%)</td>
</tr>
<tr>
<td>Transplantation</td>
<td>515 (12%)</td>
<td><strong>148 (8%)</strong></td>
<td>157 (13%)</td>
<td>64 (7%)</td>
</tr>
</tbody>
</table>

Artinyan A et al., *Cancer*, March 2010, 1367-1377
Outcomes by Race for Liver Resection or Transplantation

Artinyan A et al., *Cancer*, March 2010, 1367-1377
Cumulative Overall Survival by Race for patients who underwent Liver Transplantation (UNOS data October 1987-February 2008)

Artinyan A et al., *Cancer*, March 2010, 1367-1377
Insurance Disparities with Liver Transplantation

- Black patients are significantly less likely to receive a liver transplant than whites (up 30X less likely, OR ratio=0.03, 95% CI 0.0-0.37) \(^1\)
- Hispanics and Asian/Pacific Islanders were also less likely to receive a liver transplant but they were not statistically significant compared to whites (OR ratio=0.42, 95% CI 0.09-2.08; OR=0.33, 95% CI 0.02-4.44) respectively\(^1\)
- Patients with Private Insurance were more likely to receive a liver transplant that those patients with Medicaid \(^1\)-\(^2\)
- Black and Hispanic patients and Medicaid patients presented with HCC at a more advanced stage of disease—leading to a poorer prognosis and survival \(^1\)
- Those patients who did not receive a liver transplant were 3 times more likely to die\(^1\)

3. Robbins AS et al., *Cancer*, October 1, 2011, 4531-4539
Summary

- We have seen a doubling in the prevalence of HCC in the United States over the past 30 years.
- Early detection provides the best option for survival as it allows patients to receive a surgical intervention (Liver Transplant and Liver Resection).
- HCC is most prevalent in Asian Americans followed by African Americans (Blacks) and then Whites.
- We are seeing a dramatic increase in Hispanics with HCC compared to Whites.
- The majority of all racial/ethnic groups are diagnosed at an advanced stage of disease—leading to a poor prognosis.
- African Americans and Asian Americans are less likely to receive liver transplantation than other racial/ethnic minorities.
- African Americans have the worst survival when diagnosed with HCC and poorest survival even after LT and Liver Resection.
“...you are all new healthcare providers, so now you have the power and potential impact as clinicians to improve the lives of others...through primary care, through education, through health-promotion and through patient advocacy...there are people, rather patients out there who need you—I ask you to take care of the most vulnerable among us.”

Dr. Randy Caine