Making the Case for Liver Cancer (HCC) Screening

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Objectives

• To understand the incidence of HCC

• To understand the risk factors associated with HCC

• To understand the evidence behind why we should do surveillance for HCC
Rising Incidence of Hepatocellular Carcinoma
Burden of HCC

• Hepatocellular carcinoma (HCC) accounts for 85-90% of primary liver cancers
  • 5 year mortality is 18%

• **Fourth** leading cause of cancer mortality worldwide
  • Median survival following diagnosis is 6-20 months
  • Projected to surpass breast and CRC to become 3rd leading cause of cancer-related death in US by 2030

Figure 2. Age-Adjusted Incidence and 5-Year Survival Rates for Patients with Hepatocellular Carcinoma in the United States, 1973–2007.
Why is incidence of HCC increasing?

- Growing numbers of patients with HCV cirrhosis
- Aging of patients who acquired HCV in the 60s
  - HCV cirrhosis is the most common risk factor
    - 2-8% per year
    - HCC is the most common cause of death in HCV cirrhosis

2. World Health Organization.
Why is incidence of HCC increasing?

- Improved overall survival of patients with cirrhosis
- Increased obesity and diabetes rates
- HCC projected to continue to increase up to 2040
Global incidence of HCC: Hepatocellular carcinoma is 4th leading cause of cancer-related death worldwide.
Risk factors for HCC

• HBV
• HCV
• Alcohol

• Nonalcoholic fatty liver disease
• Diabetes

• Environmental toxins (aflatoxin)
• Cirrhosis of any etiology
Etiology of HCC around the world

HBV and HCC

• HBV is globally the most frequent underlying risk factor
• Highest in Asia (except Japan) and Africa
• Chronic HBV carriers have a 5 to 15 fold increased risk
• Up to 10-30% of HCC occurs in HBV patients WITHOUT cirrhosis
HCV is the dominant risk factor

- HBV most frequent in Asians
- HCV most frequent in whites and blacks

(N=691)
HCV and HCC

- HCV infected large numbers of adults in N. America, S and Central Europe in the 60s and 70s due to IVDA
- Infected national blood supplies until screening test developed in 1990
- HCC risk increased 17-fold in HCV+ patients compared to controls
Progression of HCV

- HCC
- Cirrhosis
- Chronic hepatitis
- HCV infection

1% (1-3%/year)
15% (10-30%)
90% (60-95%)
100%

25-30 years

References:
HCC, BMI and mortality

El-Serag H et al. Gastro. 2004;126:460-468
HCC and diabetes

El-Serag H et al. Gastro. 2004;126:460-468
Decompensation from HCV cirrhosis has not peaked yet!

Pathogenesis of HCC

Is there proof for HCC surveillance?
Criteria for cancer screening

• Screening must be effective
  ▪ Must detect cancer earlier than if cancer were detected due to symptoms
  ▪ Treatment initiated due to screening results in better outcome
• Test must be acceptable to the target population and to health care professionals
• Identifiable target population
• Screening test should be affordable

Is there proof for surveillance of HCC?

- RCT showed screening decreases mortality in HBV carriers:
  - Effective in a RCT of 18,816 Chinese patients with HBV
  - AFP + US Q 6 months vs no surveillance
  - 37% in HCC-related mortality; despite < 60% adherence to surveillance

Zhang BH et al. J Cancer Res Clin Oncol 2004;130:417-422
Screening for HCC

• Survival benefit with early screening
  ▪ Dismal prognosis after onset of symptoms (0-10% 5 yr survival)
  ▪ Dismal prognosis in patients with large liver cancer
    • Median survival is 6-9 months
• Smaller lesions may be **cured** (resection, transplantation)
  ▪ Currently only 25% are eligible for resection or liver transplantation on presentation
  ▪ HCC patients receive priority in liver transplant allocation
• Five year survival rates >70% with OLT for *early* HCC

Surveillance recommended for at-risk groups

- Specific hepatitis B carriers
  - Asian males ≥ age 40
  - Asian females ≥ age 50
  - Africans > age 20
- All cirrhotics
- US preferred at 6 month intervals
HCC surveillance is recommended by several professional society guidelines

AASLD PRACTICE GUIDELINE

Management of Hepatocellular Carcinoma: An Update

EASL–EORTC Clinical Practice Guidelines: Management of hepatocellular carcinoma

Asian Pacific Association for the Study of the Liver consensus recommendations on hepatocellular carcinoma
HCC surveillance associated with improved survival in patients with cirrhosis

Pooled Odds of 3-year Survival

I-squared = 81.6% (95%CI 73.3-87.3%)

Study	Odds Ratio (95% CI)
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Onodera 1994 [39] 3.51 (1.95 - 6.33)
Bolondi 2001 [19] 1.39 (0.94 - 2.08)
Trevisani 2002 [55] 2.09 (1.71 - 2.55)
Yu 2004 [62] 1.19 (0.98 - 1.43)
Taura 2005 [51] 1.27 (1.02 - 1.58)
Ando 2006 [17] 1.64 (1.34 - 2.00)
Tanaka 2006 [49] 1.31 (1.11 - 1.56)
Toyoda 2006 [54] 1.88 (1.62 - 2.17)
Davila 2007 [25] 1.39 (0.78 - 2.48)
Leykum 2007 [35] 2.19 (0.83 - 5.77)
Chan 2008 [22] 2.14 (1.89 - 2.42)
Pascual 2008 [40] 3.63 (2.35 - 5.62)
Silveira 2008 [44] 3.14 (1.05 - 9.38)
Stravitz 2008 [47] 2.15 (1.39 - 3.32)
Wong 2008 [58] 2.02 (1.45 - 2.81)
Kuo 2010 [34] 2.04 (1.79 - 2.32)
Noda 2010 [38] 1.42 (1.16 - 1.74)
Tong 2010 [52] 2.02 (1.25 - 3.26)
Tong 2010 [53] 1.68 (1.05 - 2.69)
El-Serag 2011 [27] 1.47 (1.09 - 1.97)
Yang 2011 [61] 4.05 (3.05 - 5.39)
Sarkar 2012 [43] 2.64 (1.33 - 5.27)

Pooled Odds of 3-year Survival
I-squared = 81.6% (95%CI 73.3-87.3%)

1.90 (1.67 - 2.17)
Hepatocellular carcinoma screening in patients with compensated hepatitis C virus (HCV)-related cirrhosis aware of their HCV status improves survival: A modeling approach

Mourad et al Hepatology 2014
HCC surveillance is underused, especially by non-subspecialists

Singal et al, J Gen Intern Med 2012
<table>
<thead>
<tr>
<th>Provider-reported barriers</th>
<th>Safety-net health system (n=77)</th>
<th>Tertiary care system (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of knowledge about guidelines</td>
<td>68.2%</td>
<td>79.1%</td>
</tr>
<tr>
<td>Competing interests in clinic</td>
<td>51.6%</td>
<td>37.4%</td>
</tr>
<tr>
<td>Lack of time in clinic</td>
<td>40.5%</td>
<td>52.8%</td>
</tr>
<tr>
<td>Difficulty recognizing at-risk patients</td>
<td>35.4%</td>
<td>30.0%</td>
</tr>
<tr>
<td>Ultrasound capacity</td>
<td>23.0%</td>
<td>10.1%</td>
</tr>
<tr>
<td>Responsibility of subspecialists &gt; PCP</td>
<td>5.3%</td>
<td>29.4%</td>
</tr>
</tbody>
</table>

Farvardin et al. Hepatology 2017
Simmons et al Clin Gastro Hep 2018
Conclusions

• Increasing incidence of hepatocellular carcinoma (HCC)
• Risk factors for HCC vary by geographic region
• Survival benefit with early screening and continued surveillance
• Compliance with existing guidelines needed with endorsement from major cancer societies
• Education is key!!
DONATE LIFE

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Give thanks. Give life.