Screening, Diagnosis, and Management of Hepatocellular Carcinoma – a Texas Epidemic

Nicole Loo, MD
Texas Liver Institute/UT San Antonio
Outline

- Why Focus on Hepatocellular Carcinoma (HCC)?
- How to Screen & Diagnose HCC
- How to Manage HCC
- New Oral HCC Therapies
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Hepatocellular Carcinoma (HCC)

- **Primary tumor of the liver** that usually develops in the setting of chronic liver disease
  - Cirrhosis (all etiologies), chronic hepatitis B without cirrhosis, and even NASH without cirrhosis (up to 13% in the VA)
Hepatocellular Carcinoma (HCC) is a Global Problem

- **Worldwide**
  - 5\textsuperscript{th} most common cancer in men
  - 9\textsuperscript{th} most common cancer in women
- **Yet, 2\textsuperscript{nd} most common cause of cancer-related deaths worldwide**
  - \(\sim746,000\) deaths in 2012
- 76\% of HCC worldwide is in Asia

http://globocan.iarc.fr/old/FactSheets/cancers/liver-new.asp
HCC is a United States Problem

- US HCC incidence has tripled since 1980
- 5th highest cause of cancer-related death in US (Behind lung, colon, pancreas, and breast)
- US HCC 5 year-survival is still low at <12%
- HCC will continue to increase until 2030 with highest increase in Hispanics > Blacks > Caucasians
In the US, Hispanics > Asians have Highest Rate of HCC (2011-2012)

To Note, California with Highest # of Hispanics

Top Latino states in 2014, by population and share

<table>
<thead>
<tr>
<th></th>
<th>Millions</th>
<th>% of population that is Latino</th>
</tr>
</thead>
<tbody>
<tr>
<td>California</td>
<td>15.0</td>
<td>48</td>
</tr>
<tr>
<td>Texas</td>
<td>10.4</td>
<td>39</td>
</tr>
<tr>
<td>Florida</td>
<td>4.8</td>
<td>39</td>
</tr>
<tr>
<td>New York</td>
<td>3.7</td>
<td>31</td>
</tr>
<tr>
<td>Illinois</td>
<td>2.2</td>
<td>28</td>
</tr>
<tr>
<td>Arizona</td>
<td>2.1</td>
<td>24</td>
</tr>
<tr>
<td>New Jersey</td>
<td>1.7</td>
<td>21</td>
</tr>
<tr>
<td>Colorado</td>
<td>1.1</td>
<td>19</td>
</tr>
<tr>
<td>New Mexico</td>
<td>1.0</td>
<td>19</td>
</tr>
<tr>
<td>Georgia</td>
<td>0.9</td>
<td>17</td>
</tr>
</tbody>
</table>

Note: Charts show the top 10 states for the number of Latinos and the share of the population that is Latino.
Source: Pew Research Center tabulations of the 2014 American Community Survey (IPUMS)
"U.S. Latino Population Growth and Dispersion Has Slowed Since Onset of the Great Recession"

PEW RESEARCH CENTER
And
Hawaii with
Highest # of
Asians

YET, Texas is #1 in HCC Rates in the USA

• By **2012**, Texas has the highest rates of HCC in the nation
  • Texas **9.71** [95% CI, 9.33–10.33] per 100,000
  • Hawaii **9.68** [95% CI, 8.22–11.33] per 100,000

Hawaii is 55.9% Asian as per the US Census in 2017. Recall Asians previously with highest HCC rate...

For Every Ethnic Group, Texas has Highest HCC Rate in 2012

Supplementary Figure 3. Age-adjusted rates for HCC by race/ethnicity in the 5 most populous US states in 2012.
Why Does Texas Have Highest HCC Rate in Every Ethnic Group?

• Decreased access to screening, diagnosis, and treatment (especially HCV treatment)?
  • TX did not adopt Medicaid expansion as part of the ACA
• Tacos:person ratio?
• Too hot to exercise here?
• More alcohol use because we are indoor more because it is too hot to exercise here?
Interestingly, South Texas (i.e. “HCC Hot Zone”) has the Most HCC

- South Texas region accounts for more than half of the incident cases of HCC in Texas overall!
- 70% of South Texas is Hispanic
- Why???

Ramirez AG et al. PLoS ONE. 2012; 7(4), e35573
Outline

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HPI: 63 yo Hispanic lady with PMH of obesity (BMI 36), type II DM (HbA1c 6.8%), HTN, hyperlipidemia, and compensated NASH cirrhosis who is here for her q6 month follow up. To discuss with her today a newly found liver lesion seen on screening ultrasound.
AASLD 2018 Recommendations for HCC Screening

- **Cirrhosis (all etiologies)**
  - HCC incidence rate is 2-8%/year
- **Chronic hepatitis B carriers who are Asian man (>40 yo), Asian woman (>50 yo), or African blacks**
  - HCC incidence rate is 0.4%-unknown
- **Chronic hepatitis B with family history of HCC**
  - HCC incidence rates are > than those without family history

AASLD recommends HCC screening every 6 months with ultrasound +/- AFP
Hepatocellular Carcinoma (HCC)

- Recommendations to perform imaging every 6 months as doubling time of HCC is 3-6 months
- Goal to **diagnose** when HCC is **early** (i.e. ≤2 cm) as more treatment options can be made available
- However, HCC is often diagnosed too late
  - Lack of symptoms of HCC until it is already advanced
  - HCC screening may not be done routinely
AFP is not PERFECT as a screening test for HCC

- **AFP**
  - Sensitivity of 66%
  - Specificity of 82%

- Assuming a 5% HCC prevalence rate in liver clinic, the positive predictive value of an **AFP of 20 ng/mL** is 41.5%
Back to the Patient

- **US**: Liver with irregular border and nodular contour. Increased echogenicity consistent with hepatic steatosis or hepatic fibrosis. **1.8 cm hyperechoic lesion in segment VIII.** Splenomegaly.

- **AFP**: 4 (normal)
Diagnosis of HCC

- Generally made by pursuing **triphasic CT of liver or MRI with GAD**.
  - **Diagnosis can be made on imaging characteristics of the lesion based on dual blood supply to the liver**

![Diagram of liver blood supply and drainage](image-url)
Diagnosis of HCC

• Generally made by pursuing **triphasic CT of liver or MRI with GAD.**
  (Diagnosis can be made on imaging characteristics of the lesion based on dual blood supply to the liver.)

  **Normal liver parenchyma** is supplied for **80% by the portal vein** and only for **20% by the hepatic artery.** Normal liver will enhance in the portal venous phase.

  **All liver tumors** get **100% of their blood supply from the hepatic artery,** so when they enhance it will be in the arterial phase.

• **There can be atypical features seen on imaging.** If there is high suspicion for HCC (ie elevated AFP, growth in size, etc) or an indeterminate concerning lesion, then can pursue biopsy.
Further Investigation

- **CT Triphasic Liver with Contrast**

  Nodular appearance of liver consistent with cirrhosis. 2.0 cm lesion seen in segment VIII with arterial enhancement and portal venous washout consistent with **hepatocellular carcinoma**.
Diagnosis of HCC

Cross-sectional imaging can be sufficient to diagnose HCC and biopsy often not needed.
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SUMMARY: 63 yo Hispanic lady with PMH of metabolic syndrome and compensated NASH cirrhosis who is found to have a 2 cm hepatocellular carcinoma as confirmed by triphasic CT of liver.

- CT CHEST non-con done and negative for metastasis
- She overall is feeling well and able to perform ADLs

What is next for treatment of her newly diagnosed hepatocellular carcinoma?
HCC Treatment

- It’s actually really complicated.
- Treatment of a liver cancer depends on number of factors:
  - Liver function
  - Performance status/age
  - Size of tumor
  - Location of tumor
  - Transplant candidacy
  - Funding
  - Your center’s expertise
HCC Staging Systems

- **BCLC**, Barcelona Clinic Liver Cancer staging
- **bm-JIS**, biomarker combined JIS
- **CLIP**, Cancer of the Liver Italian Program
- **ECOG**, Eastern Cooperative Oncology Group
- **Okuda**
- **HTLC**, Hong Kong Liver Cancer staging
- **JIS**, Japanese Integrated Staging
- **MELD**, Model for End-Stage Liver Disease
- **TNM**, Tumor-Node-Metastasis staging

2018 Modified BCLC Staging System/Treatment Strategy

Prognostic stage

Very early stage (0)
- Single <2 cm
- Preserved liver function
- PS 0

Early stage (A)
- Solitary or
- 2–3 nodules <3 cm
- Preserved liver function
- PS 0

Intermediate stage (B)
- Multinodular, unresectable
- Preserved liver function
- PS 0

Advanced stage (C)
- Portal invasion/extrahepatic spread
- Preserved liver function
- PS 11–2

Terminal stage (D)
- Not transferable HCC
- End-stage liver function
- PS 3–4

Treatment & Survival

Ablation
- >5 years

Resection
- >2.5 years

Transplant
- ≥10 months

Ablation
- 3 months

EASL CPG HCC. J Hepatol 2018; doi: 10.1016/j.jhep.2018.03.019
Treatment of HCC Requires Input from Many Specialties
Patients See Multiple Specialists, and Time to Treatment Can Be Delayed

- 6,752 patients with HCC reviewed in SEER database 1998-2007
- 22% saw 1 specialist, 32% saw 2 specialists, 39% saw 3 or more specialists

Therapeutic Delays Associated with Worse Survival

Median time to treat 1.7 months, with 31% having delays > 3 mo

N=267
HR 2.0 (95% CI 1.19 - 3.33)

Our Texas Liver Tumor Center = Multidisciplinary Care in 1 day
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2018 Modified BCLC Staging System/Treatment Strategy

TARGET POPULATION for ORAL TX

EASL CPG HCC. J Hepatol 2018; doi: 10.1016/j.jhep.2018.03.019
<table>
<thead>
<tr>
<th>Agent</th>
<th>Class</th>
<th>Line of Treatment</th>
<th>Status</th>
<th>Result</th>
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<tbody>
<tr>
<td>Sorafenib</td>
<td>TKI</td>
<td>First line</td>
<td>SOC</td>
<td>Median OS 10.7 mos</td>
</tr>
<tr>
<td>Lenvatinib</td>
<td>TKI</td>
<td>First line</td>
<td>FDA Approved 2018</td>
<td>Median OS 13.6 mos</td>
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<tr>
<td>Nivolumab</td>
<td>Anti-PD-1</td>
<td>Second line</td>
<td>FDA Approved 2017</td>
<td>Median OS 13.2 mos phase 2</td>
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<tr>
<td>Regorafenib</td>
<td>TKI</td>
<td>Second line</td>
<td>FDA Approved 2017</td>
<td>Median OS 10.6 mos</td>
</tr>
<tr>
<td>Cabozantinib</td>
<td>Anti-MET</td>
<td>Second line</td>
<td>FDA Approved 2019</td>
<td>Median OS 10.2 mos</td>
</tr>
<tr>
<td>Pembrolizumab</td>
<td>Anti-PD-1</td>
<td>Second line</td>
<td>FDA Approved 2018</td>
<td>New data 2/2019 –No improvement OS</td>
</tr>
<tr>
<td>JK-594</td>
<td>Oncolytic virus</td>
<td>First line in combination with SOR</td>
<td>Phase III</td>
<td>Q3 2018</td>
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<tr>
<td>Ramucirumab</td>
<td>Anti-VEGFR2</td>
<td>Second line</td>
<td>Phase III</td>
<td>Q2-3 2018</td>
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</table>
Conclusion

- South Texas has the highest incidence of HCC in the USA
- Please screen for HCC every 6 months in patients with cirrhosis
- HCC treatment is complicated and HCC prognosis is poor overall. Please refer early and remember us at the Texas Liver Institute/Texas Liver Tumor Center
Thank You

loo@txliver.com
Q&A/Panel Discussion

Drs. Alkhouri, Guerrero & Loo
Retrieve Lunch

Non-accredited Product Theater starts at 12:00 PM