HCC: Risk factors, surveillance and the importance of a multidisciplinary team

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I have no disclosures in regards to this presentation
Objectives

- To understand risk factors associated with HCC
- To understand surveillance and diagnosis of HCC
- To understand multidisciplinary approach for the treatment of HCC
Burden of HCC

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

- Third 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

2. World Health Organization.
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
Trends in US Cancer Mortality Rates

Annual Percent Change (1994-2003)*

*Represents the annual percent change over the time interval
National Cancer Institute Website.

Global incidence of HCC
Risk factors for HCC

- HBV
- HCV
- Alcohol
- Nonalcoholic fatty liver disease
- Diabetes
- Environmental toxins (aflatoxin)
- Hemochromatosis
- Cirrhosis of any etiology
Etiology of HCC around the world

North America

- HCV: 50%
- HBV: 20%
- Alcohol: 20%
- Other: 10%

Asia and Africa

- HCV: 70%
- HBV: 20%
- Alcohol: 10%
- Other: 10%

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 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
- HCV-related HCC is expected to peak in low-rate countries in 2010-2015
- HCC risk increased 17-fold in HCV+ patients compared to controls
Progression of HCV

El-Serag H, Rudolph KL. Gastro 2007; 132:2557-2576
Large prospective cohort study in US over 16 year period showed HCC mortality rates were 5x greater among men with higher BMI (range 35-40) compared to normals

Strong correlation between abdominal obesity, insulin resistance and hepatic steatosis

Marked steatosis with necroinflammation associated with higher fibrosis progression rates

Calle EE et al. NEJM 2003;348:1625-1638
HCC, BMI and mortality

El-Serag H, Rudolph KL. Gastro 2007; 132:2557-2576
Callee EE et al. NEJM 2003;348:1625-1638
HCC and diabetes

El-Serag H et al. Gastro. 2004;126:460-468
Annual percent change (APC) in liver cancer mortality rates by state, 2000 to 2010 by age group

Pathogenesis of HCC

Insult → Injury → Necrosis → Proliferation

Liver Cirrhosis
- Extensive scarring
- Abnormal liver nodules

Hepatocyte proliferative arrest
Stellate cell activation

Hepatocellular Carcinoma
- Well differentiated
- Moderately differentiated
- Poorly differentiated

Marked genomic instability
Loss of p53
Dysplastic nodule

Dysplastic nodule → Hyperplastic nodule

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

National Cancer Institute. Cancer screening overview
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

Is there proof for surveillance of HCC?

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

Diagnosis of HCC

- *4 phase CT/contrast enhanced MRI*
  - arterial hypervascularity
  - AND
  - venous or delayed phase washout

HCC

- YES
- No growth up to 2 yrs
- Resume q 6 month US

- NO
- Characteristic on other contrast enhanced study

Low likelihood of HCC

- US q 3 months
- No growth up to 2 yrs
- Resume q 6 month US

*4 phases: unenhanced, arterial, venous & delayed

Biopsy

- If neg, cont. to follow q 3-6 mo, consider repeat BX
Therapy in HCC

- **Surgical**
  - *Resection*
  - *Transplant: Deceased or Living Donor*

- **Locoregional Therapy**
  - Percutaneous ablation
  - *Radiofrequency Ablation (RFA)*
  - Transarterial Chemoembolization (TACE)
  - Drug eluting beads (DEB)
  - Yttrium-90 Microspheres: Radioembolization (TARE)

- **Systemic**
  - Sorafenib

- **Other**
  - Stereotactic body radiation therapy (SBRT)

* Potentially curative therapies

- “In patients with UNOS T2 HCC, and a likely waiting time > 6 months, locoregional therapy may be appropriate

- “No recommendation can be made for preferring any type of locoregional therapy to others”

Clavien PA et al Liver Transpl 2011
Quality in the Continuum of Cancer Care

Figure 1. Opportunities to Optimize Cancer Care

Processes of Care Across the Cancer Care Continuum

Types of Care

- Risk assessment
- Primary prevention
- Detection
  - Screening (Asymptomatic)
  - Appropriate Testing (Symptomatic)
- Diagnosis
  - Imaging
  - Biopsy
  - Repeat Exams
  - Laboratory Tests
  - Other Appropriate Procedures
- Cancer or precursor treatment
  - Excision
  - Surgery
  - Radiation
  - Adjuvant Chemo
  - Palliation
- Post-treatment survivorship
  - Testing
  - Follow-Up Care
  - Palliation
  - Recurrence
  - Surveillance
- End-of-life care
  - Palliative Care
  - Advanced Care Planning
  - Bereavement Support

Transitions in Care
MDT: Multidisciplinary teams

Transplant hepatology
Transplant surgery
Interventional radiology
Pathology
Radiation oncology
Oncology/Palliative Oncology
Interventional GI
Conclusions

- Increasing incidence of hepatocellular carcinoma (HCC)
- Risk factors for HCC vary by geographic region
- Survival benefit with early screening
- Unique benefits of liver transplantation (LT) for HCC
- Optimal HCC treatment requires a multidisciplinary approach
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Give thanks. Give life.