HCC Imaging and Advances in Locoregional Therapy

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-Nothing to disclose
Hepatic Imaging

- Primary imaging modalities include:
  - US
  - CT
  - MR
  - Angiography
  - Nuclear medicine
Integration of viral genes → modification of growth factor expression → early genetic alterations → late genetic alterations

Virus → chronic hepatitis → inflammatory reaction → hepatic regeneration → dysplastic nodule → Hepatocellular carcinoma → metastasis

Metabolic disease → cirrhosis

Ethanol → cirrhosis

Préneoplasia (10 to years) → dysplasia (3 to 5 years)

http://atlasgeneticsoncology.org/Deep/HepatocarcinogenesisID20055.html
Cirrhosis

- **Imaging**
  - **Ultrasound** primary screening modality
    - small echogenic coarse heterogeneous liver
    - Nodular surface
    - Regenerative nodule hypoechoic
    - Left lobe and caudate enlarge
• **CT**
  - small nodular liver with area of fatty change and fibrosis
  - recanalized umbilical vein and varices
  - splenomegaly

• **MRI**
  - Best modality to distinguish regenerative and dysplastic nodules vs HCC
Cirrhosis

• **Complications**
  
  • **Hepatocellular carcinoma**
    
    • Triple phase CT or MRI best
  
  • **Portal hypertension**
    
    • Esophageal varices with bleeding
  
    • Refractory ascites
HCC: Epidemiology

- HCC is the most common primary liver malignancy
- Worldwide incidence >600,000 cases per year
  - Liver cancer is the most rapidly increasing cancer in the U.S.
    - 19,160 new cases and 16,780 deaths in 2007
- More common in men than women (4:1)
- For resection, rate of recurrence can be as high as 50% at 2 years
  - Only 12% are eligible for resection or for transplant
  - 80%-90% of HCC cases occur in cirrhotic livers
Screening/Surveillance

- US q 6 months and AFP q 6 months is the most commonly used strategy
- Doubling time: median = 6 mo (range, 1-19 mo)
- Growth from 1 to 3 cm: 4 mo for most aggressive, 18 mo for moderately aggressive, 5 yr for indolent HCC
- Biopsy is very rarely indicated
HCC Diagnostic Criteria

- **Barcelona criteria** for imaging diagnosis of HCC accepted by AASLD and EASL
- Based on combination of size and vascular enhancement characteristics on CT or MRI
  - T1WI and T2WI on MRI not included
New OPTN/UNOS Policy for Liver Transplant Allocation

- Designed to optimize and standardize the performance of high quality imaging
- Five major issues addressed:
  - minimal tech spec for CT and MR
  - recommended contrast materials
  - mandatory diagnostic criteria for HCC
  - reporting/language requirements
  - requirements for interpretation of images at an OPTN-approved transplant center
HCC Diagnostic Criteria

- **Size category**
  - 1-2cm
  - >2cm
- **Features:**
  - arterial hyperenhancement
  - washout (hypodense relative to background liver)
  - pseudocapsule

- MRI: HCC typically hyperintense on T2WI but can be iso or hypointense
- Late arterial phase key
  - arterial hyperenhancement relative to liver
Portal venous or delayed phase
- washout - hypodense relative to liver
**Pseudocapsule**

- delayed enhancing pseudocapsule on venous/delayed phase. Represents peritumoral sinusoids and/or fibrosis.

- High overall recurrence free survival rate 4 years after LT in patients who met the restrictive Milian criteria.
- Prior to this, HCC was not a widely accepted indication for LT.
Milan Criteria for HCC

- 3 or less tumors all less than 3cm
- Single tumor <5cm

Note: Because donor livers are allocated according to the modified end-stage liver disease (MELD) scoring system, patients with HCC meeting the Milan criteria are granted a MELD “exception” of 22 points, which increases their likelihood of receiving a donor liver. If they do not receive a transplant within 3 months, such patients qualify for a further increase in MELD score—to 25.

To date the Milan criteria remain the standard of care in most UNOS regions
All HCC are categorized as OPTN class 5 lesions

<table>
<thead>
<tr>
<th>category</th>
<th>size</th>
<th>Imaging features</th>
</tr>
</thead>
<tbody>
<tr>
<td>5A</td>
<td>1-2CM</td>
<td>ARTERIAL HYPERENHANCEMENT AND WASHOUT AND PSEUDOCAPSULE</td>
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<tr>
<td>5A-g</td>
<td>1-2CM</td>
<td>ARTERIAL HYPERENHANCEMENT AND GROWTH (&gt;50% IN 6 MONTHS)</td>
</tr>
<tr>
<td>5B</td>
<td>2-5CM</td>
<td>ARTERIAL HYPERENHANCEMENT AND (WASHOUT OR PSEUDOCAPSULE OR GROWTH)</td>
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<tr>
<td>5T</td>
<td></td>
<td>PREVIOUSLY TREATED CLASS 5 LESION</td>
</tr>
<tr>
<td>5X</td>
<td>&gt;5CM</td>
<td>ARTERIAL HYPERENHANCEMENT AND (WASHOUT OR PSEUDOCAPSULE)</td>
</tr>
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</table>

Note: MELD exception not granted for solitary 5A lesions but combination of two or three 5A nodules would be eligible for transplant.
Portal Vein Thrombosis

- Tumor thrombus
  - poor prognostic indicator, ineligible for transplant

- Bland thrombus
  - common in cirrhosis, not a contraindication

- Imaging features
  - enhancement of thrombus, expanded vessel, T2 hyperintense, restricted diffusion
55 year old female
Multiple experts have stated that hepatic resection should not be entertained unless the FLR is > 40%. Liver resection is not recommended in patients with platelet counts < 100,000/μL, splenomegaly, paraesophageal varices, or other signs of clinically significant portal hypertension - See more at: http://www.cancernetwork.com/liver-gallbladder-biliary-tract-cancers/liver-transplantation-treatment-hepatocellular-carcinoma/page/0/2#sthash.rjXcGqs5.dpuf
Treatment of HCC

• **Curative Treatments**
  
  • Resection
  
  • Liver Transplant
  
  • Percutaneous ablation - RFA, Cryo, PEI, Microwave

• **Palliative Treatments**
  
  • Arterial chemoembolization / radioembolization
Percutaneous Ablation

- Percutaneous Ethanol Injection
  - common first line therapy in Japan with reported response rates of 90-100% for tumors < 2 cm
Percutaneous Ablation

- RFA

- Predictors of response include tumor size and morphology.

- 5 year survival 33-40%

Loco-regional Rx

- Numerous trials over the last 25 years comparing loco-regional Rx to conservative management demonstrating survival benefit

- Power of the studies still low

- Initial trials for unresectable HCC

- No consistent protocol

- No absolute evidence to support one specific chemotherapeutic agent
Llovet et al, Lancet 2002

• “Arterial embolization or chemo-embolization versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomized control trial”

• 112 pts
• Non-resectable HCC
• Child Pugh A or B
• Bland embo vs. chemoembo vs conservative
Survival

- Conventional TACE
  - 1 year 82%, 2 year 63%
- Bland embolization
  - 1 year 75%, 2 year 50%
- Conservative Treatment
  - 1 year 63%, 2 year 27%
debTACE (Drug-Eluting Beads)

- direct injection of spherical particulates which have been impregnated with CT agents, usually Doxorubicin or Irinotecan

- raises the local agent concentration and dwell time with less or no ischemic complications
PRECISION V TRIAL

• Only prospective, controlled, randomized study involving the safety and efficacy of deb-TACE vs c-TACE.

• 212 patients randomized to deb-TACE or conventional TACE

• Primary endpoint was tumor response (EASL) at 6 mo based on MRI
PRECISION V Trial

- 99% reduction in systemic exposure to doxirubicin
- Decreased post-embolization effect
• Although not statistically significant, deb-TACE group showed higher rates of complete response (27% vs. 22%), objective response (52% vs. 44%) and disease control (63% vs. 52%) compared to cTACE
PRECISION V TRIAL

- Patients with Child B, ECOG 1 bilobar disease and recurrent disease showed significant increase in OR ($P=0.038$) with deb-TACE

- deb-TACE group showed significant reduction in liver toxicity ($P=0.001$) and lower rates of doxorubicin related side effects ($P=0.0001$)
Your choice for a controlled distal embolization

Distal embolization may result in:
- Less opportunity for the development of collateral circulation
- Greater likelihood of tumor necrosis

Proximal embolization may result in:
- Abundant development of collateral circulation
- Restricted ability to re-treat the target lesion from the same artery
debTACE (Drug-Eluting Beads)

Potential survival benefits of deb-TACE in patients with HCC are to be reported in the next few years.
Randomized Trial of Hepatic Artery Embolization for Hepatocellular Carcinoma Using Doxorubicin-Eluting Microspheres Compared With Embolization With Microspheres Alone

This single-center, prospective study randomized patients with hepatocellular carcinoma (HCC) between bland embolization (Bead Block, Biocompatibles UK Ltd.) and transarterial chemoembolization (TACE) with drug-eluting beads (DEB-TACE; LC Bead, Biocompatibles UK Ltd.).

Patients had a diagnosis of locally advanced HCC and a bilirubin level < 3 mg/dL.

Portal vein invasion at any level was permitted as long as liver function was preserved.

Patients could also have limited extrahepatic disease.
Both treatment arms consisted of embolization with 100- to 300-μm particles, and if stasis was not achieved after the particles were administered, increasingly larger sizes of particles were administered until stasis was achieved in the target vessel.

Doxorubicin 150 mg was used for the microspheres in the DEB-TACE arm.

Of 101 randomized patients, 92 patients underwent a total of 209 embolizations during the entire study (median, 2).
Postembolization syndrome was common in both arms (88% of bland embolization and 84% of DEB-TACE patients), and adverse events were similar in both groups.

There was no difference in response rate or progression-free survival between the two groups.

Median overall survival was 19.6 months for bland embolization and 20.8 months for DEB-TACE ($P = .64$).
SIRT (Radioembolization)

Transarterial delivery of resin or glass microspheres which contain/bound with Yttrium-90

- Delivers β radiation to the tumor cells
- Direct and indirect cell death
SIRT (Radioembolization)

Candidates for SIRT:
- candidates for TACE
- poor candidates for TACE (BCLC stage B with bilobar disease)
- Failed TACE
- Contraindications for TACE (BCLC stage C or PVT)

Red Blood Cell = 6.2-8.2 µm.
61 year old vietnamese female with HBV. Preserved liver function and AFP 7404.
Y90 vs TACE

- $^{90}$Yttrium does not occlude the vessels at the arteriolar level
  - Option for repeat embolic treatment
  - Less ischemic damage
- Response rates seem to be similar (no head-to-head comparisons)
- Equivalent side effect profile
- $^{90}$Yttrium can be used in portal vein thrombosis and in more extensive disease (Sangro et al. Hepatology 2011; 54: 868-878)
Conclusion

Multiple imaging modalities available to help define liver lesions
- Ultrasound for screening
- Triple phase CT or MR for diagnostic

In patients with HCC and cirrhosis, liver transplant provides the best long term survival

Multi-specialty teams are key

Locoregional therapy serves as an important bridge to transplant or possible down staging
References


Thank you!

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Hepatitis

**Imaging**

- **Ultrasound**
  - Hepatosplenomegaly
  - Increased echogenicity of portal triads in acute hep; decreased echogenicity in chronic hep.
  - ‘starry sky’ appearance
  - GB wall thickening can occur

- Consider liver biopsy for staging
Hepatitis

- **CT:**
  - hepatosplenomegaly
  - periportal edema
  - ascites
  - lymphadenopathy
  - gallbladder wall thickening
Cirrhosis

- Hepatic fibrosis with formation of nodules that lack central vein

- Chronic sclerosing and nodular types

- Causes: Alcoholic (micronodular; most common USA, Laennec), viral (macronodular; most common worldwide), biliary cirrhosis, hemochromatosis, heart failure, wilson disease, alpha1 antitrypsin, drugs

- Symptoms include fatigue, jaundice, ascites and encephalopathy