HEPATOCELLULAR CARCINOMA (HCC) RESECTION VERSUS TRANSPLANTATION

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HEPATOCELLULAR CARCINOMA

• Hepatocellular carcinoma (HCC) is the 6th most common cancer worldwide, and the 3rd leading cause of cancer-related deaths\(^1\)
• In Asia and Sub-Saharan Africa alone, >500,000 new HCC cases develop each year\(^2\)
• The incidence of HCC is rapidly rising in Western countries and in the developing world\(^2\)
• Most HCC cases are associated with an underlying risk factor\(^1\)

Hepatocellular Carcinoma

RISING INCIDENCE OF HCC IN U.S.

Figure 2. Age-Adjusted Incidence and 5-Year Survival Rates for Patients with Hepatocellular Carcinoma in the United States, 1973–2007.

From El-Serag H. N Engl J Med 2011;365:1118-1127 (with permission)
Hepatocellular Carcinoma

WHO IS AT RISK FOR HCC?

- CHRONIC LIVER DISEASE
  - Hepatitis C
  - Fatty liver
  - Alcohol
  - Metabolic and inherited
  - Hepatitis B

- CIRRHOSIS

- LIVER CANCER (HCC)
THE 3 EPIDEMICS OF LIVER DISEASE IN U.S.

- Hepatitis C
- Fatty liver
- Alcohol
- Metabolic and inherited
- Hepatitis B

CHRONIC LIVER DISEASE

- CIRRHOSIS

- LIVER CANCER (HCC)
Hepatocellular Carcinoma

HCC - RADIOLOGIC CHARACTERISTICS
QUAD-PHASE CT OF THE ABDOMEN

Arterial Phase  Portal Venous phase
HCC - RADIOLOGIC CHARACTERISTICS
QUAD-PHASE CT OF THE ABDOMEN

Arterial Phase Enhancement
Portal Venous phase “washout”
DIAGNOSTIC CRITERIA FOR HCC
AASLD GUIDELINES (MODIFIED)

**Tumor > 1 cm** - One imaging (multi-phase CT/MRI) showing typical HCC characteristics*

* Arterial phase hypervascularity and delayed phase “washout”

Liver biopsy is not necessary for confirming diagnosis, but recommended if imaging criteria not met

*Bruix J & Sherman M - AASLD guidelines; Hepatology 2011:53:1020-1022*
Biopsy is not necessary to confirm HCC diagnosis if the lesion meets radiologic criteria in the appropriate clinical setting

*False negative biopsy common in clinical practice and may need to delay in diagnosis and treatment*

*Tumor seeding along the biopsy tract in 1-5%*

Biopsy in selected cases if atypical radiologic appearance or lack of strong risk factor for HCC
BCLC STAGING CLASSIFICATION

Stage 0
PST 0, Child-Pugh A

Very early stage (0)
Single < 2 cm, CA in situ

Stage A-C
Okuda 1-2, PST 0-2, Child-Pugh A-B

Early stage (A)
Single or 3 nodules < 3 cm, PS 0

Intermediate stage (B)
Multinodular, PS 0

Stage D
Okuda 3, PST >2, Child-Pugh C

Advanced stage (C)
Poral vein invasion, N1,M1, PS 1-2

Terminal stage (D)

Resection
Liver Transplantation
PEI/ RFA
TACE
New agents
Symptomatic Tx

5-yr survival 50-70%
3-yr survival 20-40%
1-yr survival 10-20%

Adapted from Llovet JM et al. Lancet 2003;362:1907-17
Hepatocellular Carcinoma

MULTIDISCIPLINARY LIVER TUMOR BOARD

PARTICIPANTS
- Hepatologists
- Liver surgeons
- Interventional radiologists
- Radiologist - Abdominal imaging
- Oncologists

OBJECTIVES
- Confirm diagnosis and staging
- Determine treatment strategies
Hepatocellular Carcinoma

SURGICAL TREATMENT FOR HCC
CIRRHOSIS AND LIVER FUNCTION

NON-CIRRHOTIC → RESECTION
5% in Western countries
40% in Asia

CIRRHOTIC
Child’s A
Child’s B
Child’s C

TRANSPLANT
Hepatocellular Carcinoma

HEPATIC RESECTION FOR HCC

Predictors of tumor recurrence

- Vascular invasion
- Multi-focal HCC/ satellite tumor nodules
- Tumor size > 5 cm
- Positive resection margins
- Lymph node involvement
- High alpha-fetoprotein > 2000 ng/ml
Survival following resection: Impact of portal hypertension

- No Portal HTN, normal bilirubin
- Portal HTN, normal bilirubin
- Portal HTN, increased bilirubin

HEPATIC RESECTION FOR HCC WITH CIRRHOSIS

“Ideal” candidate

- Good liver function - Child’s A cirrhosis
- No portal hypertension
  (portal hypertension suggested by varices, enlarged spleen, platelets < 100)
- Normal bilirubin
- Single lesion ≤ 5 cm
- Location of tumor in left lobe
Survival following liver transplantation and surgical resection

Survival Distribution Function

Liver Transplantation
Surgical Resection
No Treatment

Time (years)

Hepatocellular Carcinoma

LIVER TRANSPLANTATION FOR HCC
MILAN CRITERIA

1 lesion ≤ 5 cm

2 to 3, none > 3 cm

+ Absence of Macroscopic Vascular Invasion
  Absence of Extra-hepatic Spread

Patients eligible for upgrade of MELD score every 3 months on waitlist
The HCC “Metroticket” - Mazzaferro et al.

HCC Forecast Chart: Survey of 1112 patients > Milan (Pathology)


Courtesy of Dr. Vincenzo Mazzaferro, with permission
The HCC “Metroticket” - Mazzaferro et al.

HCC Forecast Chart: Survey of 1112 patients > Milan (Pathology)


“Up to 7” Criteria

Courtesy of Dr. Vincenzo Mazzaferro, with permission
The HCC “Metroticket” - Mazzaferro et al.

www.hcc-olt-metroticket.org
Predicting survival after liver transplantation in patients with HCC beyond the Milan Criteria: a retrospective, exploratory analysis

UCSF Criteria

UCSF Criteria: 1 lesion <6.5 cm, 2-3 lesions <4.5 cm, total diameter <8 cm


Courtesy of Dr. Vincenzo Mazzaferro, with permission
• To slow tumor progression and reduce risk of dropout from the waiting list – “bridge” to liver transplantation (cost-effective when waitlist time is sufficiently long > 6 months).

• “Down-staging” of HCC initially exceeding conventional or acceptable criteria*.

* Yao FY et al. Hepatology 2008;48:819-827
LOCAL REGIONAL THERAPIES FOR HCC

CHEMOEMBOLIZATION
Conventional and Drug-eluting beads

ABLATIONS

CHEMICAL
Percutaneous ethanol injection (PEI)

THERMAL
Radiofrequency ablation (RFA)
(Laparoscopic, percutaneous or open)

Microwave/ Cryo- ablation

RADIOEMBOLIZATION (YITTRIUM - 90)
TRANSCATHETER ARTERIAL CHEMOEMBOLIZATION

- Selective embolization of the hepatic arterial supply to tumor via the common femoral artery.
- Cytotoxic agent (Cis-platinum, Doxorubicin, Mitomycin-C, 5-FU) mixed with lipiodol or gelfoam particles.
- Complications include fever, abdominal pain, infection (abscess), hepatic arterial injury, hepatic decompensation.
LOCOREGIONAL THERAPY FOR HCC
TACE - DRUG-ELUTING BEADS

Tumor response (EASL criteria)

- Disease control (CR + PR + SD)
- Objective response (CR + PR)
- Complete response (CR)

DC Bead: 59 (63%)
48 (52%)
25 (27%)

p = 0.11

- SAE = NS
- Liver toxicity (ALT & AST) lower with DC beads (p< 0.001)
- Systemic effect lower with DC beads (alopecia); p< 0.001

cTACE: 56 (52%)
47 (44%)
24 (22%)

Choice of treatment based on location and size

Ideal location for Percutaneous RFA

Courtesy of Dr. Nicholas Fidelman, UCSF Radiology
Limitations of percutaneous RFA
– Tumor location

Adjacent to diaphragm

Adjacent to bowel

*Courtesy of Dr. Nicholas Fidelman, UCSF Radiology*
Limitations of percutaneous RFA – Tumor location
Adjacent to large vessel (heat-sink)
ALGORITHM FOR SURGICAL TREATMENT OF HCC

SURGICAL CANDIDATES WITH HCC AND CIRRHOSIS

SINGLE LESION

≤ 5 cm

Yes

Child’s A Bilirubin ≤ 1.1 No PHTN

Yes

No

Resection

Liver Transplantation

LOCOREGIONAL THERAPY OR PALLIATION

MULTIPLE LESIONS

2-3 lesions ≤ 3 cm

No

Yes

Locoregional therapy or palliation

Down-staging (specific criteria)
# Hepatocellular Carcinoma

## RESECTION VS TRANSPLANT FOR HCC

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<thead>
<tr>
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<th>RESECTION</th>
<th>TRANSPLANT</th>
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<tbody>
<tr>
<td>Waiting time</td>
<td>None</td>
<td>&gt; 1 year at UCSF; 20% dropout rate</td>
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<tr>
<td>Immuno -</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Suppression</td>
<td></td>
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<tr>
<td>5-yr survival</td>
<td>40-60%</td>
<td>70-80%</td>
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<tr>
<td>Recurrence of</td>
<td>&gt; 50%</td>
<td>10-20% with Milan criteria</td>
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<tr>
<td>tumor</td>
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CASE PRESENTATION

66 year-old Japanese American man with chronic hepatitis C diagnosed in 1992 during routine blood work showing abnormal liver enzymes. MRI in 1993 showed a giant hemangioma in the right lobe of the liver. A liver biopsy in 1993 showed cirrhosis. Patient felt well and never received anti-viral therapy. No surveillance imaging since that time except for one CT of the abdomen 9/2004 showing a large hemangioma in the right lobe.

On a routine follow-up physical, labs showed alpha-fetoprotein > 3000 ng/mL. Repeat same at > 3000 ng/mL.

Examination showed no spider nevi. Liver caudate lobe hypertrophy palpable 8 cm below costal margin with firm liver edge; spleen tip not palpable. No ascites or edema.
Laboratory evaluations showed:
Alpha-fetoprotein > 3000 ng/mL (2/23/2011).
WBC 4.6, HCT 46.7, platelets 164,000, creatinine 0.9, bilirubin 1.1, ALT 128, AST 96, albumin 3.8, hepatitis B surface antigen (-), hepatitis C RNA 234,480 IU/mL, alpha-fetoprotein > 3000 ng/mL (2/4/2011).

Repeat alpha-fetoprotein at UCSF = 2945 ng/mL.