TRANSARTERIAL THERAPIES FOR LIVER CANCER: HOW DECISIONS ARE MADE

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What is the best arterial treatment for HCC?

A. Bland embolization
B. Chemoembolization with 3 agents, ethiodized oil, and particles
C. Chemoembolization with 1 agent and ethiodized oil
D. Chemoembolization with drug eluting beads
E. Radioembolization with Y90 therapy
RAISE YOUR HAND QUESTION 2

What is the best method of transportation?

A. By Foot
B. Car
C. Train
D. Plane
E. Boat
ANSWER

It Depends on the Situation!

and

It Depends on Who’s Driving!
OUTLINE

Treatments for Liver Cancer

Arterial Treatment Characteristics

Patient Characteristics

Tumor Characteristics

Putting it all together
Hepatocellular Carcinoma Treatment Options:
(HCC, Hepatoma)

I. Surgery
   A. Liver Transplantation
   B. Partial Liver Resection

II. Liver Directed Treatments
   A. Catheter Based
      i. Chemoembolization/TACE
         - Poppysseed oil/doxorubicin
         - Drug eluting bead (DEB)/doxorubicin
      ii. Radioembolization (Yttrium, Y-90)
   B. Needle Ablation
      i. RFA
      ii. Microwave
   C. Radiation Therapy

III. Systemic chemotherapy
    A. Sorafenib (Nexavar)
    B. Regorafenib (Stivarga)

IV. Supportive/Palliative Care
    When or if the treatment is worse than the natural course of the disease
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   the natural course of the disease
# HCC TREATMENTS

## Transplant:

<table>
<thead>
<tr>
<th>Milan Criteria</th>
<th>UCSF Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single tumor ≤ 5.0 cm</td>
<td>Single tumor ≤ 6.5 cm</td>
</tr>
<tr>
<td>2 or 3 tumors none ≥ 3.0 cm</td>
<td>2 or 3 tumors none ≥ 4.5 cm</td>
</tr>
<tr>
<td>Childs Pugh A ≤ 50%</td>
<td>Sum of diameters ≤ 8.0 cm</td>
</tr>
</tbody>
</table>

## Resection:

<table>
<thead>
<tr>
<th>Operative risks</th>
<th>Childs Pugh A ≤ 50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td>Childs Pugh B ≤ 25%</td>
</tr>
<tr>
<td>Survival with partial liver</td>
<td>Portal HTN ≥ 10 mm Hg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Grade 2+ varices</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Plt ≤ 100 k</td>
</tr>
<tr>
<td></td>
<td>Splenomegaly</td>
</tr>
</tbody>
</table>
Systemic

sorafenib: Phase III study
median survival benefit
7.9 to 10.7 months
time to progression benefit
2.8 to 5.5 months

sorafenib (Nexavar, oral multikinase inhibitor)
regorafenib (Stivarga, oral multikinase inhibitor)
nivolumab (Opdivo, immune checkpoint inhibitor)
levatinib (Lenvima, tyrosine kinase inhibitor/VEGF Inhibitor)

Lovett et al. "Sorafenib in Advanced Hepatocellular Carcinoma"
HCC TREATMENTS

Radiation therapy:
Limited by target visibility

No contrast

Portal venous phase
IR TREATMENT OPTIONS
Mount Hood, approximately 45 min from Dotter
ARTERIAL TREATMENT OPTIONS

- TACE
- Chembo
- DEBs
- Bland Embo
- Thera-Spheres
- SIR-Spheres
NEEDLE ABLATION OPTIONS

- RFA
- Direct Injection
- IRE
- Cryoablation
- PEI
- Acetic Acid Injection
- Microwave

Dotter Interventional Institute
Which Tool in the Toolbox?/Which patient?

Mount Hood, Procedure Suite Control Room, Dotter
How to pick the right tool for the job?

Step 1: Identify specific points about the job

How much collateral liver injury can the patient tolerate?

Healthy/Unhealthy background liver

Small/Large tumor burden

Does transplant status impact your tool box?
## PATIENT BASELINE

### How sick is the patient? ECOG SCORE

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Asymptomatic (Fully active, able to carry on all pre disease activities without restriction)</td>
</tr>
<tr>
<td>1</td>
<td>Symptomatic but completely ambulatory (Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature. For example, light housework, office work)</td>
</tr>
<tr>
<td>2</td>
<td>Symptomatic, &lt;50% in bed during the day (Ambulatory and capable of all self care but unable to carry out any work activities. Up and about more than 50% of waking hours)</td>
</tr>
<tr>
<td>3</td>
<td>Symptomatic, &gt;50% in bed, but not bedbound (Capable of only limited self-care, confined to bed or chair 50% or more of waking hours)</td>
</tr>
<tr>
<td>4</td>
<td>Bedbound (Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair)</td>
</tr>
<tr>
<td>5</td>
<td>Death</td>
</tr>
</tbody>
</table>
CIRRHOSIS BASELINE

How bad is the underlying liver cirrhosis? CHILDS-PUGH SCORE

Table 2. Definition and criteria of Child-Pugh classification

<table>
<thead>
<tr>
<th>Points</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>Minimal</td>
<td>Advanced (coma)</td>
</tr>
<tr>
<td>Ascites</td>
<td>Absent</td>
<td>Controlled</td>
<td>Refractory</td>
</tr>
<tr>
<td>Serum bilirubin (mg/dl)</td>
<td>&lt;2.0</td>
<td>2.0–3.0</td>
<td>&gt;3.0</td>
</tr>
<tr>
<td>Serum albumin (g/dl)</td>
<td>&gt;3.5</td>
<td>2.8–3.5</td>
<td>&lt;2.8</td>
</tr>
<tr>
<td>Prothrombin activity (%)</td>
<td>&gt;70</td>
<td>40–70</td>
<td>&lt;40</td>
</tr>
</tbody>
</table>

Total scores: 5–6, Child-Pugh class A; 7–9, Child-Pugh class B; 10–15, Child-Pugh class C

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
<th>1 and 2 Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (5-6 pts)</td>
<td>Well Compensated</td>
<td>100% and 85%</td>
</tr>
<tr>
<td>B (7-9 pts)</td>
<td>Significant Compromise</td>
<td>80% and 60%</td>
</tr>
<tr>
<td>C (10+ pts)</td>
<td>Decompensated</td>
<td>45% and 35%</td>
</tr>
</tbody>
</table>

Hepatology 2000; 31: 840-845.
# TUMOR BURDEN

How bad is the cancer? CLIP SCORE

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score</th>
<th>Median Survival (mo)</th>
<th>1 and 2 Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child–Pugh stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor morphology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum α-fetoprotein (ng/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Portal vein thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>36</td>
<td>84% and 65%</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>22</td>
<td>66% and 45%</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>8.5</td>
<td>45% and 17%</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>7</td>
<td>36% and 12%</td>
</tr>
<tr>
<td></td>
<td>4-6</td>
<td>3</td>
<td>9% and 0%</td>
</tr>
</tbody>
</table>

Hepatology 2000; 31: 840-845.
TUMOR BURDEN

How bad is the cancer? Okuda Score

Table 1 Definition of the Okuda staging system for hepatocellular carcinoma

<table>
<thead>
<tr>
<th>Points</th>
<th>Tumour size</th>
<th>Ascites</th>
<th>Albumin (g/dl)</th>
<th>Bilirubin (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt;50% of liver</td>
<td>No</td>
<td>≥3</td>
<td>&lt;3</td>
</tr>
<tr>
<td>1</td>
<td>&gt;50% of liver</td>
<td>Yes</td>
<td>&lt;3</td>
<td>≥3</td>
</tr>
</tbody>
</table>

Okuda stage I, 0 points; Okuda stage II, 1 or 2 points; Okuda stage III, 3 or 4 points.

<table>
<thead>
<tr>
<th>Okuda Stage</th>
<th>Median Survival (mo)</th>
<th>1 and 2 Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>23</td>
<td>68% and 48%</td>
</tr>
<tr>
<td>II</td>
<td>6.7</td>
<td>36% and 13%</td>
</tr>
<tr>
<td>III</td>
<td>2.9</td>
<td>21% and 10%</td>
</tr>
</tbody>
</table>
HCC TREATMENTS

Summarizing the 10 + scoring systems

<table>
<thead>
<tr>
<th>Liver function</th>
<th>Tumor Burden</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Small</td>
</tr>
<tr>
<td>Good</td>
<td>Go for cure</td>
</tr>
<tr>
<td>Bad</td>
<td>Be careful</td>
</tr>
</tbody>
</table>

Soulen, Michael—HUP
Which Tool in the Toolbox?

Oregon Coast, 2 hours from Dotter
HCC TREATMENTS

How to pick the right tool for the job?

Step 2: Identify specific points about the tool

How much collateral liver injury is there when you use the tool?

Advantages/disadvantages of one tool over another?

How effective is the tool at big or small lesions?

How good is your team with that specific tool?
HCC TREATMENTS

Ablation

Limited size: 3-5 cm

Control ablation of adjacent liver

Impact of Adjacent Structures

Ascites

Access the lesion

Biopsy vs. Ablation (Skill)
HCC TREATMENTS

Radioactive Particles - Yttrium ($^{90}$Y)

SirSphere/TheraSphere

“Practice Run”

T-Bili limit of 1.5-2.0

ECOG 0-1

Arterial supply

Cost

Pure beta emitter

Half life - 64.1 hours

Energy max - 2.27 MeV, mean 0.93 MeV

<table>
<thead>
<tr>
<th>RANGE</th>
<th>Air</th>
<th>Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max</td>
<td>9.6 m</td>
<td>11 mm</td>
</tr>
<tr>
<td>Mean</td>
<td>3.7 m</td>
<td>2.5 mm</td>
</tr>
</tbody>
</table>
HCC TREATMENTS

Embolic agents +/- Drug Eluting Beads (DEBs)

Doxorubicin: up to 150 mg

Embolic Load

T-Bili limit of 2.0-3.0

ECOG 0-2

Arterial supply

Cost

DC/LC, LUMI beads

BTG

Quadraspheres
Merit Medical

HydroPearl
Terumo

Oncozene
CeloNova

Optisphere
Medtronic
HCC TREATMENTS

Chemoembolization (East Coast)

3 Drug Chemotherapy: cisplatin, doxorubicin, mitomycin C

Iodinated Poppy-seed oil

Embolic Particles added at end of treatment

T-Bili limit of 2.0-3.0

ECOG 0-2

Arterial supply

Overnight stay, hydration

PVA: irregular clumping, non-uniform occlusion, proximal occlusion

Round PVA: semi-spherical, self-affinity, non-uniform occlusion, less targeted occlusion
HCC TREATMENTS

Chemoembolization (West Coast)

Single agent chemotherapy: doxorubicin

Iodinated Poppy-Seed Oil

No Permanent Embolic

T-Bili limit of 2.0-3.0

ECOG 0-2

Arterial supply

Overnight/Same day
HCC TREATMENTS

How to pick the right tool for the job?

Step 3: Is there a tool “combo” that works well?

- chemoembolization + ablation = approaching surgical results
- systemic + locoregional therapy = limited, but improving data
HCC TREATMENTS

Summary Characteristics of IR tools
(in my hands anyway)

Best survival overall: combination chemoembolization and ablation

Biggest Hammer: $^{90}\text{Y}$

2${}^{\text{nd}}$ Biggest Hammer: DEB

Chembo experience: EAST vs WEST

3 drug (CAM) + Ethiodol + PVA  doxorubicin/ethiodol, no particles

Gentle therapy: WEST (doxorubicin/ethiodol, no particles)
Putting them together

Unnamed waterfall, outside Bend Oregon, 3 hours from Dotter
Best survival overall: combination chemoembolization and RFA
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Best survival overall: combination chemoembolization and RFA
EXAMPLE

2009 (9 months out)  9/2015 (6 years out)
EXAMPLE

Best survival overall: combination chemoembolization and RFA

With “touch up” treatments 9/2018 (9 years out)
Biggest Hammer: $^{90}\text{Y}$
EXAMPLE

10 cm tumor, branch portal vein involved, 
Childs-Pugh A, CLIP 2
HCV, not a resection candidate
7/2012

Biggest Hammer: $^{90}$Y
EXAMPLE

Initial diagnosis: 7/2012
(CLIP II: 17% 2 year)

Y90-dominant treatment
3 Chembo “touch ups”
Still in follow up 10/2015

Biggest Hammer: $^{90}\text{Y}$
Climbing AFP, new lytic bone lesion, stable liver disease
5/2016
Initially on sorafenib until progression (11/2017)  
Then to Nivolumab 19 cycles, last seen 8/31/2018  

AFP from 10/2012-to last month
EXAMPLE

Treatment at age 85-91 (and still going)

Situation can change during therapy and follow up

If what your doing is working: keep it up

If it’s not working: CHANGE!
CONCLUSIONS

Underlying Patient Condition Affects Outcome
CONCLUSIONS

Underlying Patient Condition Affects Outcome

Extent of Tumor Burden Affects Outcome
CONCLUSIONS

Underlying Patient Condition Affects Outcome

Extent of Tumor Burden Affects Outcome

Choice of IR Tool
Involves Patient, Tumor, and MDs Features
CONCLUSIONS

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In Many Cases:
NOT A COMPLETE CURE!
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Slows Progression of Disease
CONCLUSIONS

Underlying Patient Condition Affects Outcome

Extent of Tumor Burden Affects Outcome

Choice of IR Tool Involves Patient, Tumor, and MDs Features

In Many Cases: NOT A COMPLETE CURE!

Slows Progression of Disease

Dynamic Process: Keep up with the situation
There may not be a “best” in all situations
There may be a “best” in a specific situation