LIVER SURGERY I

Med 5 Refresher Course (Surgery) 2013/14
19 Jun 2013

Dr Sunny Cheung

Outline

- Liver anatomy and nomenclature of liver resection
- Management of HCC
- Pre-operative work-up
- Intraoperative consideration
- Loco-regional treatment
Liver Anatomy – Morphology

- Tumor factor
  - Number, site, size, PV status
  - Liver transplantation: Milan criteria
- Liver factor
- Patient factor
  - Co-morbidity, ASA Class
  - Performance status
- Expertise available

Division of HBP Surgery, Department of Surgery, Prince of Wales Hospital, CUHK
### Couinaud’s Segment - Functional

- Each segment has its own portal & hepatic arterial supply and biliary and hepatic venous drainage

---

### Brisbane 2000 Nomenclature of Liver Anatomy and Resections

<table>
<thead>
<tr>
<th>Couinaud Segments</th>
<th>Anatomical Terms</th>
<th>Resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sg 5-8</td>
<td>R Liver</td>
<td>R Hepatectomy</td>
</tr>
<tr>
<td>Sg 2-4</td>
<td>L Liver</td>
<td>L Hepatectomy</td>
</tr>
<tr>
<td>Sg 5,8</td>
<td>R Anterior Section</td>
<td>R Anterior Sectionectomy</td>
</tr>
<tr>
<td>Sg 6,7</td>
<td>R Posterior Section</td>
<td>R Posterior Sectionectomy</td>
</tr>
<tr>
<td>Sg 2,3</td>
<td>L Lateral Section</td>
<td>L Lateral Sectionectomy</td>
</tr>
<tr>
<td>Sg 4</td>
<td>L Medial Section</td>
<td>L Medial Sectionectomy</td>
</tr>
</tbody>
</table>
Segmentectomy & Extended Resections

Segmental Anatomy on CT

- A) Level of hepatic veins
- B) Portal vein bifurcation
- C) Below hepatic hilus
MANAGEMENT OF HCC

Presentation

- Symptomatic
- Usually advanced disease and unresectable

- Screening detected
- High risk group:
  - Chronic HBV / HCV carrier
  - Alcoholic
  - Metabolic disease
  - Haemochromatosis
  - NAFLD
Screening in high risk group

- How?
  - 6-monthly USG +/- AFP
    - USG: Sensitivity = 58-89%, Specificity > 90%
    - AFP alone is too non-specific and not sensitivity enough
    - 10-20% early stage HCC has abnormal AFP
    - Fluctuating AFP level might reflect flares of HBV / HCV infection, exacerbation of underlying liver disease
    - AFP only adds 6-8% of cases not identified by USG
- Is it useful?
  - Single RCT in China in HBV carrier
  - Reduced HCC-related mortality to 37%

Recall Policy / Non-invasive Diagnosis

AFP is dropped from the diagnostic scheme
CT scan

Radiological hallmark of HCC
• Contrast uptake in arterial phase
• Washout in venous / late phase

(a) The HCC presents as a hypodense lesion in the plain scan.
(b) This becomes hyperdense during the arterial phase.
(c) The lesion has a variable attenuation during the portal venous phase.
(d) Hypodense during the delayed phase.

Yu 2004 Clinical Radiology

Dual-tracer PET in Metastatic HCC

• $^{18}$F-FDG PET has false negative rated up to 40-50%
• $^{11}$C-acetate complement deficiency

$^{18}$F-FDG PET/CT in the detection of metastatic HCC

Ho 2007 J Nucl Med
Staging

- AJCC – prognosis after resection
  - TNM – extent of tumor
  - Not considering liver function
- Okuda & CLIP
  - Tumor and liver function status considered
- BCLC
  - Link staging with treatment strategy
  - Allows prognostic prediction and treatment allocation

Updated BCLC Staging system 2011

<table>
<thead>
<tr>
<th>WHO Performance Status stages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
</tr>
<tr>
<td>Fully active, normal life, no symptoms</td>
</tr>
<tr>
<td>Stage 1</td>
</tr>
<tr>
<td>Minor symptoms, able to do light activity</td>
</tr>
<tr>
<td>Stage 2</td>
</tr>
<tr>
<td>Ambulatory and capable of all self-care but unable to carry out any work activities, can walk about more than 50% of waking hours</td>
</tr>
<tr>
<td>Stage 3</td>
</tr>
<tr>
<td>Capable of only limited self-care, confined to bed or chair more than 50% of waking hours</td>
</tr>
<tr>
<td>Stage 4</td>
</tr>
<tr>
<td>Cannot carry on any self-care. Totally confined to bed or chair</td>
</tr>
</tbody>
</table>

EASL Journal of Hepatology 2012 56:908-943
Work-up for Hepatectomy

- Patient: co-morbidity
- Tumor: number, size, location
- Liver function assessment
  - Child’s grading
  - Platelet count
  - Evidence of portal hypertension
  - Indocyanine Green (ICG) clearance test
    - Residual at 15 min < 14% able to undergo major hepatectomy
    - LI-MON – spectrophotometer
- Size of future liver remnant (CT Volumetry)
  - Normal liver = 30%
  - Diseased liver = 40%
    - Cirrhosis, steatosis
    - Chemotherapy-related (irinotecan-CASH, oxaliplatin-sinusoidal dilatation)

Investigation - Suspect Liver Tumor

- Blood test
  - LFT, CBC (platelet), PT / INR
  - Hepatitis serology: HbsAg, Anti-HCV
  - Tumor marker: AFP +/- CEA
- Imaging
  - USG
  - Triphasic contrast CT scan: tumor and volume of FRL
  - CXR
- Indocyanine green test
- Cardiopulmonary assessment
Intra-operative Consideration

- Vascular Control
  - Inflow:
    - Pringle’s maneuver (portal triad clamping)
    - Ischaemic-reperfusion injury – intermittent clamp
    - Hilar dissection and ligation of ipsilateral inflow vessels
  - Outflow: Low CVP < 5mmHg
- Instruments:
  - Operative USG
  - Dissecting device: CUSA
  - Haemostatic device: TissueLink, Bipolar diathermy etc
  - Haemostatic adjuncts
    - Tisseal / Floseal (thrombin / fibrinogen)

Neoadjuvant / Adjuvant treatment

- Neoadjuvant treatment
  - No benefit, but even poorer survival
- Adjuvant treatment
  - $^{131}I$ and interferon – showed some benefit but sample size too small
  - STORM study – sorafenib, pending results
Liver Transplant

- Within Milan Criteria
  - Solitary tumor up to 5cm
  - Multifocal: up to 3 tumor nodules and each nodule <3cm
- Survival comparable to other transplant candidates without HCC
- Good for cirrhotic patients
  - Treat both tumor and cirrhosis
- But …
  - Shortage of graft / deceased donor, esp in Asia
  - Long waiting time on transplant waiting list, dropout due to progressive disease is common
  - Living donor liver transplant might be a solution but need to balance the risk to donor, even if the risk is small
  - Overall tumor recurrence rate is 8–20%, usually within first 2 years after transplant
  - Survival after recurrence was poor (median < 1 year)

Hepatectomy vs Transplantation for HCC within Milan criteria

- Although partial hepatectomy had higher overall recurrence rate (48 vs 10%), overall survival at 5-year were comparable
- Hepatectomy can therefore be considered an equivalent alternative to transplantation for HCC within Milan criteria, unless patient has prohibitive liver function
LOCAL ABLATION THERAPY

What is local ablation therapy

- Destruction of tumor cells with local treatment (c.f. tumor resection)
- Modalities available
  - Chemical
  - Ethanol injection
  - Thermal
  - RFA – better local control than PEI, esp tumor > 2cm
  - Microwave ablation
  - Generate heat to induce tumor necrosis
  - Open, laparoscopic or percutaneous route
Selection Criteria

- Small tumor
- Solitary or oligometastases
- Tumor not favorable for hepatectomy
- HCC
- Liver metastasis
  - Colorectal liver metastasis
  - Neuroendocrine tumor

Cool-tip™ RF Ablation System

<table>
<thead>
<tr>
<th>Electrode</th>
<th>Exposure (cm)</th>
<th>Duration (min)</th>
<th>Min Diameter (cm)</th>
<th>Mean Height (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td>2</td>
<td>6</td>
<td>2.3</td>
<td>2.6</td>
</tr>
<tr>
<td>Single</td>
<td>3</td>
<td>12</td>
<td>3.1</td>
<td>3.7</td>
</tr>
<tr>
<td>Cluster</td>
<td>2.5</td>
<td>12</td>
<td>4.2</td>
<td>4.5</td>
</tr>
</tbody>
</table>

Tissue response to heat

- Destruction RNA/Mitochondria
- Collagen denatures
- Thermal injury starts

[Diagram showing the Cool-tip™ RF Ablation System and its parameters]
Factors Influencing Successful RFA

- Ability to ablate all viable tumor tissue
- Create adequate tumor-free margin
- Target diameter of ablation zone should be 2cm > tumor diameter
- The largest tumor should ≤ 3cm in longest axis

\[ D^* = d + 2\text{cm} \]

<table>
<thead>
<tr>
<th>Tumor Size</th>
<th>Tumor Type</th>
<th>Complete Response Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 3cm</td>
<td>HCC</td>
<td>90%</td>
</tr>
<tr>
<td>&gt;3cm</td>
<td>HCC</td>
<td>48%</td>
</tr>
<tr>
<td>≤ 3cm</td>
<td>Liver met</td>
<td>87%</td>
</tr>
<tr>
<td>&gt;3cm</td>
<td>Liver met</td>
<td>53%</td>
</tr>
</tbody>
</table>

Limitation

- Tumor not in close proximity to major vessels or bile duct
- Heat-sink effect
  - Presence of large (≥3mm) abutting vessels
  - Heat-loss mediated by perfusion-mediated tissue cooling
  - Decrease complete tumor necrosis by 50%
- Bile duct injury
Survival Rate of RFA in Selected Patients

Table 4: Studies Reporting 5-year Survival Rate for Early-Stage HCC Treated with RF Ablation as Sole First-Line Non-surgical Treatment

<table>
<thead>
<tr>
<th>Study and Disease Classification</th>
<th>No of Patients</th>
<th>1-year</th>
<th>5-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lencioni et al, 2005</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child-Pugh A</td>
<td>146</td>
<td>100</td>
<td>95</td>
</tr>
<tr>
<td>Child-Pugh B</td>
<td>43</td>
<td>89</td>
<td>84</td>
</tr>
<tr>
<td>Child-Pugh C</td>
<td>271</td>
<td>97</td>
<td>87</td>
</tr>
<tr>
<td>Child-Pugh A*</td>
<td>90</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>(Yi et al, 2007)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child-Pugh A</td>
<td>399</td>
<td>NA</td>
<td>76</td>
</tr>
<tr>
<td>Child-Pugh B</td>
<td>140</td>
<td>NA</td>
<td>76</td>
</tr>
<tr>
<td>Yeo et al, 2009</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCC resectable</td>
<td>97</td>
<td>NA</td>
<td>76</td>
</tr>
<tr>
<td>HCC non-resectable</td>
<td>145</td>
<td>NA</td>
<td>76</td>
</tr>
</tbody>
</table>

* Any four of the following criteria: Child-Pugh class C cirrhosis; HCC size > 2 cm; presence of satellite lesions; absence of major liver functional reserve; and absence of significant portal hypertension.

RFA has comparable overall survival to resection in small HCC (<5cm)
Considered as curative treatment in small but unresectable HCC

Microwave Ablation
Microwave Ablation vs RFA

- Different heating mechanism
  - RFA: relies on current flow through patient, to induce tissue ions agitation
  - MWA: EM energy radiates into tissue through antenna to induce water molecule to oscillate
- Larger zone of active heating
- Higher intra-tumoral temp
- Larger tumor ablation volumes in shorter ablation times
- Improved convection profile
- MW is less affected by vessels in proximity to tumor (Heat-sink effect)

The Latest Model of 2.45 GHz Device
Example of Microwave Ablation

Recurrent HCC with previous right posterior sectionectomy

1 month after MVA
3 months after MVA

Division of HBP Surgery, Department of Surgery, Prince of Wales Hospital, CUHK

6 months after MVA

Division of HBP Surgery, Department of Surgery, Prince of Wales Hospital, CUHK
Efficacy of Microwave Ablation in HCC

- Complete Ablation Rate = 88-100%
- PWH Experience
  - 26 patients received microwave ablation from Mar 2009 – Jan 2011
  - Median tumor size = 3.8 (2.0 to 6.0) cm
  - Median OT time = 118 (65-250) min
  - Complication rate = 19%
  - At median FU of 14 months, 11 patients (42% developed recurrence)
  - 5 patients (19%) next to ablation site (local recurrence)
  - Mean survival = 25 months

Transarterial Treatment
**TACE**

- TACE
  - Intra-arterial infusion of cytotoxic agent followed by embolization of tumor-feeding vessels
  - Strong cytotoxic and ischaemic effect
  - 2 RCT confirmed beneficial results as palliative treatment
  - BCLC: doxorubicin
  - HKU: cisplatin
  - Repeat every 2 months
  - Balance the risk of liver dysfunction / failure

**Selective Internal Radiation**

- Infusion of radioactive substance
- Microspheres containing Yttrium-90
- Due to hypervascularity of HCC, $^{90}$Y preferentially delivered to tumor-bearing area
- Selectively emit high-energy, low-penetration radiation to tumor
- Pre-procedure test with TcMAA (Technetium Macroaggregated Albumin)
- Pulmonary shunting < 10%, T/N liver uptake ratio > 2
- Median survival = 12 to 17.2 months
- Liver related toxicity = 20%
- Mortality = 3%
Systemic treatment

- Adriamycin (doxorubicin)
  - 10% response rate
  - Toxicity – no proven survival benefit in RCT
- Sorafenib
  - Targeted therapy
  - Proven in RCT to improve survival (~2 months)
  - Very expensive