Surgical management of HCC

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Global distribution of HCC and staging systems

WEST
1. Italy (Milan, CLiP)
2. France
3. Spain (Barcelona)

EAST
1. Japan (JIS)
2. China (CUPI)
3. Korea (Hangzhou)
The arsenal of treatments for HCC

- Liver transplantation (15%)
- Ablative treatments (TACE, PEI, etc) (15%)
- Sorafenib (15%)
- Best supportive care (15%)
- Resection (15%)
Comparison of OS and DFS among available treatment options

**Table 2. Treatment Modalities for Hepatocellular Carcinoma**

<table>
<thead>
<tr>
<th>Treatment Modality</th>
<th>Survival</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatectomy</td>
<td>41%-74%</td>
<td>70% (5 yrs)</td>
</tr>
<tr>
<td>OLT</td>
<td>&gt;70% (5 yrs)</td>
<td>&lt;15% (5 yrs)</td>
</tr>
<tr>
<td>RFA/PEI</td>
<td>70% (5 yrs) lesions &lt;2 cm</td>
<td>2%-50% (3 yrs)</td>
</tr>
<tr>
<td>TACE/Y90</td>
<td>20%-60% (2 yrs)</td>
<td>TACE is a noncurative treatment; response rates, 6% to 60%</td>
</tr>
<tr>
<td>Sorafenib</td>
<td>Median survival is 3 months longer than with placebo</td>
<td>Time to progression is 3 months longer than with placebo</td>
</tr>
</tbody>
</table>

OLT, orthotopic liver transplantation; PEI, percutaneous ethanol injection; RFA, radiofrequency ablation; TACE, transarterial chemoembolization; Y90, yttrium-90.

Determinants of surgical management

- Size of tumour
- Future liver remnant
- Liver function
Surgical management of HCC

- **20%**
  - No cirrhosis
    - Resection
    - Transplantation
    - Bridging therapies

- **80%**
  - Cirrhosis
    - Resection
    - Transplantation
    - Bridging therapies
      - TACE
      - RFA
      - Alcohol injection
      - Other
Non cirrhotic HCC

- The treatment of choice for non cirrhotic HCC is resection
  
  Perioperative mortality (0–6%) and morbidity (8–40%) of these patients are rather low

- Five-year and median overall survival rates after resection of non-cirrhotic conventional HCC are 67% and 137 months (95% confidence interval [CI], 89–184 months)

- 5-year and median recurrence-free survival rates are 55% and 108 months

Contraindications to resection among non cirrhotic HCC

- The contraindications to resection include:
  1. All the contraindications for a hepatectomy
  2. NASH related HCC: associated with impaired functional reserve and extent of resection should be considered with caution
  3. Size of HCC is not a contraindication for resection, but affects outcomes as a prognostic factor


Liver transplantation in Non cirrhotic HCC

- Non resectable HCC and
  - absence of macro vascular invasion
  - absence of extra hepatic spread

- Or patients with previously resected HCC in a non-cirrhotic liver and
  - have intrahepatic recurrence of HCC >12 m after
  - no evidence of macro vascular invasion or extra hepatic spread

Salvage transplantation

Indian J Surg 2012 74(1):100-117
Cirrhosis

BCLC

0

A

Milan criteria

Within

Transplantation

Without

Bridging therapies

Re-assess

Re-section
Ideal for resection patient

- Has a solitary HCC confined to the liver
- No radiographic evidence of invasion of the hepatic vasculature
- No evidence of portal hypertension
- Well-preserved hepatic function.
Stage 0 and A with PH

- **Established treatment LT or RFA**
  - However
    - Long waiting time
    - Drop out
    - Limited availability of Donors
    - High costs

- **Alternatively LR and RFA**

- **Surgery with better OS than RFA in single early HCC > 2cm**

- **In single very early HCC < 2cm**
  - LR gives similar OS with RFA

  *J Gastrointest Surg 2011; 15: 311-320*
  *Hepatol Res 2013; 43: 853-864*

*J Hepatol 2012; 56: 412-418*
BCLC A-B multiple HCCs not suitable for LT

- Established treatment RFA or TACE

However

Liver resection can give better long term results than TACE alone

- Ann Surg 2002; 235: 373-382
- J Gastrointest Surg 2012
BCLC B Large HCC > 5cm

- Established treatment TACE

However

Surgery is as safe as TACE with better OS in many series

NS survival benefit between preoperative TACE + surgery in comparison with surgery alone


J Gastrointest Surg 2009; 13: 1313-1320
BCLC HCC stage C with Macrovascular invasion

- selected patients with PVTT may benefit from more aggressive treatment modalities

*World J Gastroenterol 2016 August 28; 22(32): 7289-7300*

- PV resection vs. Thrombectomy showed non significant difference regarding morbidity and mortality

- Same regarding long term results such OS and DFS

Survival outcomes were far more better than no treatment or TACE

*World J Gastroenterol. 2015 Oct 21;21(39):11185-98*
Anatomical versus non-anatomical resection for hepatocellular carcinoma

S. Marubashi1, K. Gotoh1, H. Akita1, H. Takahashi1, Y. Ito2, M. Yano4, O. Ishikawa4 and M. Sakon1

1Department of Surgery and 2Centre for Cancer Control and Statistics, Osaka Medical Centre for Cancer and Cardiovascular Diseases, Osaka, Japan
Correspondence to: Dr S. Marubashi, Department of Surgery, Osaka Medical Centre for Cancer and Cardiovascular Diseases, 1-3-3 Nakamichi, Higashinari-ku, 537-8511, Osaka, Japan (e-mail: s-marubashi@umc.ac.jp)

Background: The optimal surgical resection method in patients with HCC to minimize the risk of local recurrence has not yet been determined. The aim of this study was to compare the prognosis following anatomical versus non-anatomical hepatic resection for hepatocellular carcinoma (HCC).

Methods: Consecutive patients with HCC without macroscopic vascular invasion, treated by curative resection between 1981 and 2012 at Osaka Medical Centre, were included in this retrospective study. The outcomes of patients selected by propensity score matching were compared.

Results: Some 1102 patients were included, 577 in the anatomical and 525 in the non-anatomical resection group. By propensity score matching, 329 patients were selected into each group. Demographic, preoperative and tumour variables were similar between the propensity score-matched groups, including tumour size, tumour multiplicity, α-fetoprotein level and 15-min indocyanine green retention rate at 15 min. The incidence of microvascular invasion was higher in the matched anatomical resection group (P = 0.048). Stratified analysis of recurrence-free and overall survival rates revealed no statistically significant differences between the two propensity score-matched groups (P = 0.704 and P = 0.381 respectively). There was also no significant difference in the early recurrence rate within 2 years after resection between these groups (P = 0.726). Subset analysis of the early recurrence-free survival rate in patients with and without microvascular invasion revealed no significant differences between the groups (P = 0.312 and P = 0.479 respectively).

Conclusion: The resection method had no impact on the risk of HCC recurrence or survival.
Anatomical vs Non-anatomical

**Pros for anatomical**
- Reduce risk of local/intrahepatic recurrence

**Cons of anatomical**
- Technically challenging (lap?)
- Time consuming
- Alteration of hilar structures affecting subsequent transplantation

**Pros for non-anatomical**
- Parenchyma sparing
- Feasible laparoscopically

**Cons of non-anatomical**
- Blood loss
- Increased risk of local/intrahepatic recurrence

Meta analysis with conflicting results based on observational studies
Need for large randomized trials

Anatomical vs Non anatomical

HCV

AFP

Billirubin

Tumor size 2-5

Prognostic factors of outcomes

Table 4 Univariate analysis of prognostic tumour factors

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of tumours (multi)</th>
<th>Tumour size (larger)</th>
<th>Differentiation (less)</th>
<th>Vascular invasion (histopathology)</th>
<th>Intrahepatic metastases</th>
<th>Capsule invasion</th>
<th>Portal vein invasion</th>
<th>Capsule presence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fukuda et al.</td>
<td>NS</td>
<td>NS (30 mm)</td>
<td>NS</td>
<td>NEG</td>
<td>NEG</td>
<td>NS</td>
<td>a</td>
<td>a</td>
</tr>
<tr>
<td>Pandey et al.</td>
<td>NEG</td>
<td>NEG (size limit)</td>
<td>NEG</td>
<td>NEG</td>
<td>a</td>
<td>NS</td>
<td>a</td>
<td>a</td>
</tr>
<tr>
<td>Hashimoto et al.</td>
<td>NS</td>
<td>NS</td>
<td></td>
<td></td>
<td></td>
<td>a</td>
<td>a</td>
<td>a</td>
</tr>
</tbody>
</table>

Table 3 Univariate analysis of prognostic patient factors

<table>
<thead>
<tr>
<th>Study</th>
<th>Inc age</th>
<th>Male</th>
<th>Cirrhosis</th>
<th>Child A</th>
<th>HBs Ag+</th>
<th>HCV Ab+</th>
<th>Lower Alb</th>
<th>Higher ICGR15</th>
<th>Higher AFP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fukuda et al.</td>
<td>NS</td>
<td>NEG</td>
<td>NEG</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NEG</td>
<td>NS</td>
</tr>
<tr>
<td>Pandey et al.</td>
<td>NS</td>
<td>NS</td>
<td>NEG</td>
<td>N/A</td>
<td>NS</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>NS</td>
</tr>
<tr>
<td>Hashimoto et al.</td>
<td>NS</td>
<td>NS</td>
<td>a</td>
<td>NS</td>
<td>NS</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
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<tr>
<td>Shimada et al.</td>
<td>NEG</td>
<td>a</td>
<td>a</td>
<td>NS</td>
<td>NEG</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
</tr>
<tr>
<td>Zhou et al.</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
</tr>
<tr>
<td>Zhou et al.</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
</tr>
<tr>
<td>Hanazaki et al.</td>
<td>a</td>
<td>a</td>
<td>NEG</td>
<td>POS</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
</tr>
<tr>
<td>Shirabe et al.</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>a</td>
<td>NEG</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
</tr>
<tr>
<td>Lee et al.</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>a</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Analysis not performed or not specifically identified.
NS, not statistically significant; POS, positive prognostic factor; NEG, negative prognostic factor; N/A, not applicable; Child A, Child–Pugh class A liver function; HBs Ag+, positive hepatitis B surface antigen; HCV Ab+, positive hepatitis C antibody; ICGR15, indocyanine green dye retention at 15 minutes; AFP, alpha fetoprotein.
Recurrence post resection

Hepatic Re-resection Versus Transarterial Chemoembolization for the Treatment of Recurrent Hepatocellular Carcinoma after Initial Resection: a Systematic Review and Meta-analysis

Di-Ya Wang¹, Lei Liu²&, Xing-Shun Qi³&, Chun-Ping Su⁴, Xue Chen³, Xu Liu³, Jiang Chen³, Hong-Yu Li³, Xiao-Zhong Guo³*

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log[Hazard Ratio]</th>
<th>SE</th>
<th>Total</th>
<th>Total</th>
<th>Weight</th>
<th>Hazard Ratio</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>log[Hazard Ratio]</td>
<td>SE</td>
</tr>
<tr>
<td>Hirokawa 2011</td>
<td>-0.92</td>
<td>0.78</td>
<td>10</td>
<td>12</td>
<td>1.7%</td>
<td>0.40 [0.09, 1.84]</td>
<td></td>
</tr>
<tr>
<td>Ho 2012</td>
<td>-0.48</td>
<td>0.25</td>
<td>54</td>
<td>254</td>
<td>8.4%</td>
<td>0.62 [0.38, 1.01]</td>
<td></td>
</tr>
<tr>
<td>Imaoka 1995</td>
<td>-0.45</td>
<td>0.19</td>
<td>31</td>
<td>142</td>
<td>10.3%</td>
<td>0.64 [0.44, 0.93]</td>
<td></td>
</tr>
<tr>
<td>Lee 1995</td>
<td>0.01</td>
<td>0.45</td>
<td>25</td>
<td>12</td>
<td>4.2%</td>
<td>1.01 [0.42, 2.44]</td>
<td></td>
</tr>
<tr>
<td>Shimamura 1994</td>
<td>-0.45</td>
<td>0.43</td>
<td>11</td>
<td>34</td>
<td>4.5%</td>
<td>1.06 [0.27, 1.48]</td>
<td></td>
</tr>
<tr>
<td>Takemura 2014</td>
<td>-0.17</td>
<td>0.1</td>
<td>249</td>
<td>251</td>
<td>13.3%</td>
<td>0.84 [0.69, 1.03]</td>
<td></td>
</tr>
<tr>
<td>Tanai 2012</td>
<td>0.01</td>
<td>0.16</td>
<td>23</td>
<td>89</td>
<td>11.3%</td>
<td>1.01 [0.74, 1.38]</td>
<td></td>
</tr>
<tr>
<td>Ueno 2009</td>
<td>-0.44</td>
<td>0.24</td>
<td>9</td>
<td>13</td>
<td>8.7%</td>
<td>0.64 [0.40, 1.03]</td>
<td></td>
</tr>
<tr>
<td>Umeda 2011</td>
<td>-1.17</td>
<td>0.26</td>
<td>29</td>
<td>38</td>
<td>8.1%</td>
<td>0.31 [0.19, 0.52]</td>
<td></td>
</tr>
<tr>
<td>Wang 2014</td>
<td>-0.74</td>
<td>0.1</td>
<td>128</td>
<td>339</td>
<td>13.3%</td>
<td>0.48 [0.39, 0.58]</td>
<td></td>
</tr>
<tr>
<td>Yamamoto 2013</td>
<td>-0.31</td>
<td>0.17</td>
<td>32</td>
<td>144</td>
<td>11.0%</td>
<td>0.73 [0.53, 1.02]</td>
<td></td>
</tr>
<tr>
<td>Yang 2009</td>
<td>-0.79</td>
<td>0.38</td>
<td>11</td>
<td>24</td>
<td>5.3%</td>
<td>0.45 [0.22, 0.96]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td></td>
<td></td>
<td>612</td>
<td>1352</td>
<td>100.0%</td>
<td>0.64 [0.52, 0.79]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.08; Chi² = 34.82, df = 11 (P = 0.0003); I² = 68%
Test for overall effect: Z = 4.14 (P < 0.0001)

Clear survival benefit
ALPPS and HCC

- Two stage hepatectomy

Morbidity after second surgery 20%-60%

Drop out rate 8%-31%

5 year OS is reported to be 51%

ALPPS reported

Morbidity (bile leakage and sepsis) 16-64%

Mortality (Hepatic insufficiency) 12-23%

Long term oncological outcomes are not yet available

HPB. 2013; 15:483-491
ALPPS and HCC

- Open ALPPS for HCC in cirrhotic liver has been described in few case reports
- Laparoscopic ALLPS feasible by experts
- Robotic ALPPS may have place in HCC

Large scale studies needed to further evaluate
“Laparoscopic segments”
Laparoscopic Approach for HCC

**Louisville USA 2008**
- Solitary lesions less than 5cm
- Located in segments (II, III, IVb, V and VI)
- Away from hepatic hilum and IVC
- Non-compensated cirrhosis absolute contraindication

**Morioka Japan 2014**
- Size limit over passed however lesions >10 cm relative contraindication
- Location over passed
- PVTT safe and feasible in selected patients by highly experts surgeons
- PH contraindication for resection > 3 segments
Laparoscopic Approach for HCC

Advantages / Disadvantages

- Decrease rate of bleeding / need for transfusion
- Minimize post operative ascites
- Reduce adhesion formation
- Decrease LOS
- Decrease morbidity

- Issue with reproducibility
- Learning curve > 60
- Requiring expertise in both liver surgery and advanced laparoscopy
- Available in HPB tertiary centers

No differences regarding surgical margins and Long term results (OS and DFS)

*Ann Surg Oncol. 2013; 20:1203-1215*
Robotic approach for HCC

- All liver segments surgery
- Complex hilar dissection
- Bilioenteric reconstruction
No difference regarding mortality morbidity LOS and negative margin rate

Operative time significantly longer for RLR irrespective type of hepatectomy (minor or major)

However lack of prospective comparative studies in HCC field
Innovative surgical approach for HCC

- 3-D surgical planning software
  1. Simulating surgery
  2. Calculating liver volumes
- PVE and stem cell application – CD133+ bone marrow derived stem cells (role in the process of tissue regeneration)

Need for further studies to ensure safety and effectiveness

WJ Surg Oncol 2013, 11:192
Innovative surgical approach for HCC

- Robotic augmented reality (AR)-assisted liver resection

- Fusion between live images and synthetic computer-generated patient-specific images is defined as augmented reality (AR)

**Fig. 4** Augmented reality-guided robotic segmentectomy. AR allowed for a correct dissection of the tumor (displayed in green) with accurate identification of liver vascularization.
Suitable for LT patient

- with liver disease (usually cirrhosis) who would not tolerate liver resection
- who have a solitary HCC ≤5 cm in diameter or up to three separate lesions none of which is larger than 3 cm (within Milan criteria)
- no evidence of gross vascular invasion
- no regional nodal or distant metastases.
Events in the evolution of LTx for HCC
Transplantation criteria for HCC

1. Pre 1990’s: all HCC transplanted
2. PB: Resectable better off transplantable
3. Milan criteria
4. UCSF: extended criteria
5. BCLC

Disappointing results

Improvement of LTx results
Transplantation for HCC


Recommendations for liver transplantation for hepatocellular carcinoma: an international consensus conference report.

Clavien PA, Lesurtel M, Bossuyt PM, Gores GJ, Langer B, Perrier A; OLT for HCC Consensus Group.

Collaborators (110)

**Transplantation for HCC**

### Summary of recommendations and statements

<table>
<thead>
<tr>
<th>Assessment of candidates with HCC for liver transplantation</th>
<th>Level of evidence</th>
<th>Strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. When considering treatment options for patients with HCC, the BCLC staging system is the preferred staging system to assess the prognosis of patients with HCC</td>
<td>2B (P)</td>
<td>Strong</td>
</tr>
<tr>
<td>2. The TNM system (7th edn) including pathological examination of the explanted liver, should be used for determining prognosis after transplantation with the addition of assessment of macrovascular invasion</td>
<td>2B (P)</td>
<td>Strong</td>
</tr>
<tr>
<td>3. Either dynamic CT or dynamic MRI with the presence of arterial enhancement followed by washout on portal venous or delayed imaging is the best non-invasive test to make a diagnosis in cirrhotic patients suspected of having HCC and for presurgical staging</td>
<td>1B (D)</td>
<td>Strong</td>
</tr>
<tr>
<td>4. Portal staging should include CT of the chest, and CT or MRI of the abdomen and pelvis</td>
<td>3B (D)</td>
<td>Strong</td>
</tr>
<tr>
<td>5. Tumour biopsy is not required in cirrhotic patients considered for liver transplantation who have high-quality dynamic CT or MRI findings typical for HCC and a lesion larger than 1 cm according to current AASLD guidelines</td>
<td>1B (D)</td>
<td>Weak</td>
</tr>
<tr>
<td>6. For patients with lesions smaller or equal to 10 mm, non-invasive imaging does not allow an accurate diagnosis and should not be used to make a decision for or against transplantation</td>
<td>1B (D)</td>
<td>Strong</td>
</tr>
</tbody>
</table>

### Criteria for listing candidates with HCC in cirrhotic livers for LDLT

- LDLT is acceptable for HCC patients who have an expected 5-year survival similar to comparably staged patients receiving a deceased donor liver. In LDLT, careful attention should be given to psychosocial considerations regarding both donor and recipient.
- LDLT must be reserved for patients with high-risk disease and maximise recipient outcome.
- LDLT is not recommended for patients with HCC outside the accepted criteria for LDLT, retransplantation for graft failure is justified.
- LDLT is not recommended for patients with high-risk disease and maximise recipient outcome.

### Role of LDLT

- LDLT is acceptable for HCC patients who have an expected 5-year survival similar to comparably staged patients receiving a deceased donor liver. In LDLT, careful attention should be given to psychosocial considerations regarding both donor and recipient.
- LDLT must be reserved for patients with high-risk disease and maximise recipient outcome.
- LDLT is not recommended for patients with HCC outside the accepted criteria for LDLT, retransplantation for graft failure is justified.
- LDLT is not recommended for patients with high-risk disease and maximise recipient outcome.

### Post-transplant management

- LDLT is acceptable for HCC patients who have an expected 5-year survival similar to comparably staged patients receiving a deceased donor liver. In LDLT, careful attention should be given to psychosocial considerations regarding both donor and recipient.
- LDLT must be reserved for patients with high-risk disease and maximise recipient outcome.
- LDLT is not recommended for patients with HCC outside the accepted criteria for LDLT, retransplantation for graft failure is justified.
- LDLT is not recommended for patients with high-risk disease and maximise recipient outcome.

### Level of evidence for each recommendation

- Level of evidence 1A: Systematic review of randomised clinical trials
- Level of evidence 1B: Systematic review of non-randomised clinical trials
- Level of evidence 2A: Prospective cohort studies or registries
- Level of evidence 2B: Retrospective cohort studies or registries
- Level of evidence 3B: Consensus statements or clinical guidelines
- Level of evidence 5: Expert opinion

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**Note:** The information provided is based on the assumption that the document is a medical report or guideline on liver transplantation for hepatocellular carcinoma (HCC). The specific details and recommendations may vary based on the source of the document and the current clinical practice guidelines. Always consult the latest and authoritative sources for the most accurate and up-to-date information.
Does the type of donor graft matter?

**Liver Transplantation: East versus West**

Akash Shukla, Hemant Vadeyar, Mohamed Rela, Samir Shah

Institute of Liver Diseases, HPB Surgery and Transplantation, Global Hospital – Superspeciality and Multiorgan Transplant Centre, 35, Dr. E. Borges Road, Hospital Avenue, Mumbai 400012, Maharashtra, India

<table>
<thead>
<tr>
<th>Center</th>
<th>Criteria</th>
<th>Type of donor</th>
<th>Recurrence-free survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milan, Italy</td>
<td>Diameter ≤ 5 cm if single lesion</td>
<td>DDLT 100%</td>
<td>75% 4 yr survival</td>
</tr>
<tr>
<td></td>
<td>Diameter ≤ 3 cm if multiple lesions and number of lesions ≤ 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UCSF, USA</td>
<td>Diameter ≤ 6.5 cm if single lesion or</td>
<td>DDLT 93%</td>
<td>75% 5 yr survival</td>
</tr>
<tr>
<td></td>
<td>Diameter ≤ 4.5 cm if ≤ 3 lesions if total diameter ≤ 8 cm</td>
<td>LDLT 7%</td>
<td></td>
</tr>
<tr>
<td>Asan, Korea</td>
<td>Diameter ≤ 5 cm</td>
<td>LDLT 100%</td>
<td>76.3% 5 yr survival</td>
</tr>
<tr>
<td></td>
<td>No. of lesions ≤ 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No gross vascular invasion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kyoto, Japan</td>
<td>Diameter ≤ 5 cm</td>
<td>LDLT 100%</td>
<td>86.7% 5 yr survival</td>
</tr>
<tr>
<td></td>
<td>No. of lesions ≤ 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PIVKA-II ≤ 400 mAU/ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fukuoka, Japan</td>
<td>Diameter or number not limited</td>
<td>LDLT 100%</td>
<td>74% 3 yr survival</td>
</tr>
<tr>
<td></td>
<td>No gross vascular invasion or extrahepatic disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tokyo, Japan</td>
<td>Diameter ≤ 5 cm</td>
<td>LDLT 100%</td>
<td>94% 3 yr survival</td>
</tr>
<tr>
<td></td>
<td>No of lesions ≤ 5</td>
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</table>
Is it Time to Reconsider the BCLC/AASLD Therapeutic Flow-Chart?

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Journal of Surgical Oncology 2010;102:868–876

Resection  Liver Transplantation  RFA  TACE  Sorafenib  Symptomatic treatments

Curative treatments  Palliative treatments
BCLC Evolution

BCLC Stages

0

A

A1

A2

A3

A4

SR

SR/LT

LT

LT

(1999)

SR

SR

SR/LT

LT

LT

(2005)

SR

SR

SR/LT

LT

LT

(2011)

SR

SR

SR/LT

LT

LT

(Current)

LT

LT+TACE

LT+TACE

LT+TACE

LT+TACE

LT (if possible)

TACE+RFA/PEI

TACE+PAI/TA RE

TACE+SR (if resectable)

TACE+MWA

TACE

TACE

TACE

New agents

New agents

Sorafenib

SR+Sorafenib

SR+Sorafenib

LT (if possible)

HAC/PEI

HAC+RT

SC

SC

SC

SC

Potential/Best Strategies

Therapeutic Strategies

Oncotarget. 2017 Jan 15. doi: 10.18632
Is LT effective among patients presented outside the Milan Criteria?

**Liver Transplantation for Advanced Hepatocellular Carcinoma after Downstaging Without Up-Front Stage Restrictions**

William C Chapman, MD, FACS, Sandra García-Aroz, MD, Neeta Vachharajani, BS, Kathryn Fowler, MD, Nael Saad, MD, Yijing Lin, MD, PhD, Jason Wellen, MD, FACS, Benjamin Tan, MD, Adeel S Khan, MD, FACS, MB Majella Doyle, MD, FACS

**CONCLUSIONS:** Patients with beyond—Milan criteria HCC who are otherwise candidates for LT should undergo aggressive attempts at downstaging without a priori exclusion. This highly selective approach allows for excellent long-term results, similar to patients presenting with earlier-stage disease. (J Am Coll Surg 2017;i:1–12. Published by Elsevier Inc. on behalf of the American College of Surgeons.)
CONCLUSIONS: In initially transplantable HCC-cirr patients, ITT survival was better in group PLT compared with group LR. SLT was feasible in only a third of patients who recurred after LR. Post SLT, short and long-term outcomes were comparable with PLT. Better patient selection for the "resection first" approach and early detection of recurrence may improve outcomes of the SLT strategy.
Outcomes of salvage LT in HCC

In favour of Salvage

HCC resection combined with LTx

- **Resection** of HCC – follow up – if recurrence – **Salvage Transplantation** (ST)

- Resection as bridge to Transplantation

  List the patient for Tx – Resection to keep him within Tx criteria – Followed by Tx

- Resection as selection tool for Transplantation

  Resection-List the patient and do a preemptive Tx

- Resection as Down staging tool for Transplantation

  As outside criteria resection then follow up and Tx
<table>
<thead>
<tr>
<th>Type of treatment for HCC recurrence in LT patients</th>
<th>No. of patients</th>
<th>Median survival(^1) (mo) (weighted mean ± SD)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loco-regional treatments for resectable local recurrence of HCC</td>
<td></td>
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</tr>
</tbody>
</table>
| Surgery | 27 | 42 ± 24.45 | Bates et al\(^{[38]}\)  
Kornberg et al\(^{[58]}\)  
Pfiffer et al\(^{[54]}\)  
Kim et al\(^{[67]}\)  
Chen et al\(^{[77]}\)  
Sommacale et al\(^{[74]}\)  
Tan et al\(^{[80]}\)  
Kim et al\(^{[67]}\)  
Pfiffer et al\(^{[54]}\)  
Carr\(^{[99]}\)  
Chen et al\(^{[77]}\)  
Yamagami et al\(^{[64]}\) |
| TACE | 40 | 11.2 ± 8.81 | |
| Systemic treatments for unresectable, advanced, multifocal recurrence of HCC | | | |
| Sorafenib | 76 | 12.1 ± 9.95 | Tan et al\(^{[80]}\)  
Yoon et al\(^{[65]}\)  
Pfiffer et al\(^{[54]}\)  
Staufer et al\(^{[76]}\)  
Sposito et al\(^{[79]}\)  
Pfeifferberger et al\(^{[78]}\)  
Alsina et al\(^{[73]}\)  
Waidmann et al\(^{[54]}\)  
Gomez-Martin et al\(^{[48]}\)  
Weimann et al\(^{[63]}\)  
Staufer et al\(^{[76]}\)  
Sotiropoulos et al\(^{[58]}\)  
Lee et al\(^{[84]}\)  
Kim et al\(^{[67]}\)  
Kim et al\(^{[67]}\)  
Pfiffer et al\(^{[54]}\)  
Yoon et al\(^{[82]}\)  
Sposito et al\(^{[79]}\) |
| Sorafenib + mTOR | 68 | 18.2 ± 6.53 | |
| Systemic chemotherapy | 35 | 5.79 ± 2.7 | |
| Best supportive care | 54 | 3.3 ± 2.12 | |
Recurrence after LT: the end of the line?

Recurrence of hepatocellular carcinoma after liver transplantation: Is there a place for resection?

Fernandez-Sevilla E, Allard MA, Selten J, Golse N, Vibert E, Sa Cunha A, Cherqui D, Denis C, Adam R.
King’s HCC management

HCC referral (new patients)
- OP review
- Cirrhosis
- P/S
- Cause of HCC
- Staging

HCC MDM
- Hepatologist
- Radiologist
- **Surgeon**
- Oncologist
- CNS
- Palliative care

Patients on pathway of treatment

Decision to treat
Outcomes of multimodal management

Multimodality Therapy and Liver Transplantation for Hepatocellular Carcinoma: A 14-Year Prospective Analysis of Outcomes

Rajesh Ramanathan, MD,a Amit Sharma, MD,a David D Lee, MD,a Martha Behnke, PhD,a Karen Bornstein, RN,a R Todd Stravitz, MD,a Malcolm Sydnor, MD,b Ann Fulcher, MD,b Adrian Catterall, MD,a Marc P Posner, MD,a and Robert A Fisher, MDa

Figure 1.
Survival from diagnosis of HCC in patients contraindi cated for liver transplantation
HCC without cirrhosis: resection is the gold standard unless otherwise contraindicated

HCC with cirrhosis:
- Early cirrhosis (C-P:A), solitary nodule: resection
- Early cirrhosis within Milan criteria (CP:A-B): LTx
- Early cirrhosis without Milan criteria (CP:A-B): Bridging therapies
- Significant cirrhosis (C-P:B-C) or out of Milan criteria: down staging/bridging therapies and re-assess

Severe cirrhosis: Symptomatic treatment irrespective of the tumour

Dynamic evolution of indications for LR and LT

HCC is a disease best served by HPB centers where a MDM approach can take place