Resection of liver limited resectable metastases – Upfront, neoadjuvant and repeat hepatectomy

Dr Chan Chung Yip
MBBS, M.Med(Surgery), MD, FAMS, FRCSEd

Senior Consultant and Head
Department of Hepatopancreatobiliary and Transplant Surgery
Singapore General Hospital
Associate Professor (Adj), Duke-NUS Medical School

ESMO Preceptorship Programme – GI Tumours
Singapore 14-16 November 2017
Introduction

• Resection of colorectal liver metastasis (CRLM) is required for long term survival

• 15-25% will present with synchronous CRLM

• 40-50% will develop CRLM within 3 years of resection of primary tumour

• 25% of patients with CRLM are eligible for surgical extirpation
Chronology of chemotherapy for mCRC

- Meta-analysis JCO 1998: Bolus 5-FU/LV 11.3
- Meta-analysis JCO 1998: Infusional 5-FU/LV 12.1
- van Cutsem JCO 2001: Capecitabine 13.2
- Douillard Lancet 2000: FOLFIRI 17.4
- Kalofanos Ann Oncol 2005: Bolus 5-FU/LV + oxali or irino 17.6
- Goldberg JCO 2004: Oxaliplatin + infusional 5-FU/LV 19.5
- Tournigand JCO 2004: FOLFIRI → FOLFOX vs. FOLFOX → FOLFIRI 21.5
- Falcone JCO 2007: FOLFOXIRI 22.6
- Maindralt-Goebel ASCO 2007: FOLFOX7 → 5-FU+LV → FOLFOX7 → other agents 24.6
<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Operative Mortality %</th>
<th>1-yr Survival %</th>
<th>3-yr Survival %</th>
<th>5-yr Survival %</th>
<th>10-yr Survival %</th>
<th>Median Survival (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gayowski 1994[10]</td>
<td>204</td>
<td>0</td>
<td>91</td>
<td>–</td>
<td>32</td>
<td>–</td>
<td>33</td>
</tr>
<tr>
<td>Fong 1999[7]</td>
<td>1001</td>
<td>2.8</td>
<td>89</td>
<td>57</td>
<td>36</td>
<td>22</td>
<td>42</td>
</tr>
<tr>
<td>Adam 2001[14]</td>
<td>335</td>
<td>1</td>
<td>91</td>
<td>66</td>
<td>48</td>
<td>30</td>
<td>52</td>
</tr>
<tr>
<td>Choti 2002[12]</td>
<td>226</td>
<td>1</td>
<td>93</td>
<td>57</td>
<td>40</td>
<td>26</td>
<td>46</td>
</tr>
<tr>
<td>Tomlinson 2007[18]</td>
<td>612</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>17</td>
<td>44</td>
</tr>
<tr>
<td>Rees 2008[19]</td>
<td>929</td>
<td>1.5</td>
<td>–</td>
<td>–</td>
<td>36</td>
<td>23</td>
<td>43</td>
</tr>
<tr>
<td>House 2010[15]</td>
<td>563</td>
<td>1</td>
<td>–</td>
<td>69</td>
<td>51</td>
<td>37^a</td>
<td>64</td>
</tr>
<tr>
<td>Nathan 2010[20]</td>
<td>949</td>
<td>0.9</td>
<td>–</td>
<td>65</td>
<td>45</td>
<td>22</td>
<td>52</td>
</tr>
</tbody>
</table>

^8-yr survival.

Table 2: Results of Liver Resection for Colorectal Metastases
Surgical resection of colorectal liver metastasis in patients with expanded indications: a single-center experience with 501 patients.


- 501 patients with 545 liver resections over 15 year period comparing classic with expanded indications

- Expanded indications: lesions > 10cm (n=14), bilateral deposits (n=194), ≥ 4 metastasis (n=140), extra-hepatic disease (n=73)

- 52% of patients

- 5 year survival: 45% vs 34%, 10 year survival: 36 vs 24% (p=0.0009)

- ≥ 4 metastases and extra-hepatic disease predict poor outcome
Can we improve survival with chemotherapy?
Role of adjuvant chemotherapy in resectable CRLM

- Robust data on role of systemic chemotherapy for resected stage III and unresectable stage IV cancer
- Data on role of adjuvant chemotherapy for resected CRLM is scant
- 4 randomized trials, 2 published
- Both did not show difference in overall survival, Portier et al trial showed disease free survival benefit
- Poor accrual, small sample size
Role of adjuvant chemotherapy in resectable CRLM

• Several large retrospective studies

• All reported overall and DF survival benefit for adjuvant 5-FU


• No difference in overall or DF survival
Peri-operative and Neoadjuvant Chemotherapy

• Survival benefits from pre-hepatectomy chemotherapy have not been established

• Retrospective studies show improved survival with adjuvant therapy but not with neoadjuvant therapy. Increased post operative complications

• Only 1 randomized trial (EORTC Intergroup trial 40983)
  - Norlinger B et al. Lancet Oncol 2013
EORTC Intergroup Trial 40983

- 364 patients randomized to surgery alone or surgery with perioperative FOLFOX 4 chemotherapy

- Median follow-up 8.5yrs

- Non-statistically significant trend in 5yr PFS favouring chemotherapy group (38% vs 30%, HR 0.81, p=0.068)

- 5yr OS similar: 51% vs 48% (HR 0.88, 95% CI 0.68-1.14)
Peri-operative and Neoadjuvant Chemotherapy

• Early treatment of systemic disease

• Allow biology of disease to declare itself

• In vivo assessment of response to chemotherapy

• While already resectable, lesions treated with neoadjuvant chemotherapy may benefit from further downsizing to facilitate increased rates of margin negative as well as parenchymal sparing resections
Progression on chemotherapy

• Marker for aggressive tumour biology

• Uncommon, 5-15% of patients

• Development of new lesions strongest predictor of poor post-hepatectomy outcome

• 5 yr survival in pts with >3 mets that progressed – 8%

• Prognostic impact of progression in form of growth of pre-existing lesion less clear

Allen et al. J Gastrointest Surg 2003
Can prehepatectomy chemotherapy identify pts who will unlikely benefit from hepatectomy?

- Relatively few patients experience disease progression while receiving short duration of contemporary chemotherapy
  - 11/171 pts (7%) exhibited progressive disease in response to FOLFOX (EORTC Intergroup Trial 40983. Lancet 2008)

- Median progression-free survival for metastatic unresectable cancer exceeds 6 months in most phase III trials

- Extended durations of chemotherapy treatment would be required to identify those patients with interval disease progression
How useful is prehepatectomy chemotherapy an in-vivo test of response?

• Response to chemotherapy before hepatic resection will help determine optimal post hepatectomy chemotherapy

• 14% and 9% of patients whose disease was downsized from unresectable to resectable CLM responded to second and third lines of treatment when first-line chemotherapy failed. Adam R et al. Ann Surg 2004
Disease progression on pre-hepatectomy chemotherapy may render previously resectable CLM unresectable, thereby preventing opportunity for long term survival?

• EORTC 40983: 364 pts ≤ 4 mets assigned to liver resection with or without perioperative chemotherapy

• 67/182 pts assigned to chemo had objective response

• 11 progressed, 8 of whom no longer resectable

• 83% resected vs 84% in surgery alone group
Chemotherapy induced liver injury

- Irinotecan – Steatosis, Chemotherapy Associated SteatoHepatitis (CASH)

- Oxaliplatin: Sinusoidal injury (Sinusoidal Obstruction Syndrome- SOS, “blue liver syndrome”)

- Bevacizumab: Impairment of liver regeneration (anti-VEGF)
Does preoperative chemotherapy increase the morbidity and mortality after surgery?

- EORTC Intergroup trial 40983, overall complication increased from 16-25%, rate of hepatic complications from 9-15%. No change in mortality. Norlinger et al, Lancet 2008

- Multicentric cohort study showing significantly higher complication rate 24% vs 37% in patients subjected to neoadjuvant chemotherapy for resectable lesions. Adam R et al. Ann Surg 2010

- In the setting of extended surgical resection, may contribute to development of small for size syndrome and fatal liver failure
Can neoadjuvant chemotherapy help select patient for type of surgical resection?

• Recurrence following liver resection is expected

• Shift from anatomical resection to parenchymal sparing strategies to improve subsequent resectability

• Trade off: Higher risk of margin positive resection
Margin status remains an important determinant of survival after surgical resection of colorectal liver metastases in the era of modern chemotherapy.  


Optimal morphological response
Margin status remains an important determinant of survival after surgical resection of colorectal liver metastases in the era of modern chemotherapy.  


• Pathological response: Area of residual viable tumour cells within each metastatic lesion as percentage of total tumour surface area
• Minor response: 0-49%
• Major response: ≥50%
• Multiple nodules: Mean of response in each individual nodule
Margin status remains an important determinant of survival after surgical resection of colorectal liver metastases in the era of modern chemotherapy.  


- 52 of 378 resections (14%) R1 resections.
- 246 (65%) synchronous lesions. No of mets median=2, mean=3
- 5yr OS R0 vs R1 resection: 55% and 26%
- Survival benefit a/w negative margins greater in patients with suboptimal morphological response (5yr OS: 62% vs 11%, P=0.007); patients with optimal response (3yr OS rate: 92% vs 88%, P=0.917)
- Greater in patients with minor pathological response (5yr OS: 46% vs 0%, P=0.002); patients with major response (5yr OS: 63% vs 67%, P=0.587)
Margin status remains an important determinant of survival after surgical resection of colorectal liver metastases in the era of modern chemotherapy. 


- Optimal radiological response: Multiple wedge resections (parenchymal sparing)

- Suboptimal radiological response: Anatomical resections
Dilemma - The disappearing metastasis

Nov 2011

Feb 2012
The disappearing metastases

- Complete clinical response from chemotherapy to sites of CLM obviates the need for surgical extirpation of these sites?

- Benoist S et al reported the recurrence of disease at site of unresected disappearing lesions in 23 of 31 lesions (74%). *J Clin Oncol* 2004.

- Tanaka et al reported similar findings with recurrence in 11 of 27 lesions (41%) at median of 14 months f/u. *Ann Surg* 2009.
Predictors of patient with at least one metastases that disappears

• Small size <3cm
• Multiple lesions > 3
• Longer duration of chemotherapy

The disappearing metastases

• PET does not reliably predict pathological response

• 34 lesions in 14 patients had resolution of PET positivity after prehepatectomy chemotherapy. 29 (85%) had viable tumour on microscopic examination

• 40% of complete pathological response have radiologically evident lesions
The disappearing metastases

- Good quality MRI to identify “missing metastases”

- <10% of pts have complete radiological response of all liver metastases, hence most patients will undergo surgery for residual disease

- IOUS identifies additional lesions that alter surgical planning in a substantial number of patients

- Extended prehepatectomy chemotherapy induces pathological changes in surrounding non-tumour bearing liver that reduces sensitivity of both IOUS and visual examination to detect small lesions
Fong Clinical Risk Score

- Nodal status of primary
- DFI from primary to discovery of liver mets <12mths
- Number of tumours >1
- Preop CEA > 200ng/ml
- Largest tumor > 5cm

Ann Surg 1999
Effect of neoadjuvant chemotherapy in patients with resectable colorectal liver metastases

Zhu DX et al. PlosOne 2014

• Retrospective analysis of 466pts between 2000 and 2010
• Pts divided into pts who received neoadj chemo (n=121) and pts who had adj chemo (n=345)
• No diff in morbidity, 30-day mortality and 5yr survival (52% vs 48%)
• Risk factors: Primary tumour T4, ≥4 mets, largest met ≥5cm, serum CEA ≥5ng/ml
• Low risk 0-2 factors, high risk 3-4 factors
• Low risk group no survival benefit from neoadjuvant chemo, high risk group survival benefit (5yr 39% vs 33%, p=0.028)
Liver resection for multiple colorectal liver metastases with surgery up-front approach: Bi-institutional analysis of 736 cases.


- 625 resectable pts and 111 initially unresectable (ie converted) – 1993 to 2008
- Upfront resectable pts did not receive any preop-chemotherapy and few had adjuvant chemotherapy
- Patients divided into 3 groups: Group A 1-3 tumours (n=493), Group B 4-7 tumours (n=141), Group C 8 or more tumours (n=102)
- 5 year overall and recurrence free survival: Group A: 51% and 21%, Group B: 56% and 29%, Group C: 33% and 1.7%
- Prognostic factors for DFS: Extrahepatic disease, positive surgical margin, nodal involvement of primary, tumour number ≥4, size >5cm, CEA>200ng/mL, primary site (rectum)
- Prognostic factors for OS: Node positive primary tumour, EHD, size ≥5cm, positive margin
Should neoadjuvant chemotherapy be given in resectable colorectal liver metastases?

• Are there sufficient risks of possible poor tumor biology such that addition of one additional factor (ie progression on chemotherapy) would be sufficient to not offer resection?

• Does the patient have diabetes, obesity of other factors that compromise liver health, such that any degree of liver injury from preoperative chemotherapy might be significantly deleterious?

• Though resectable, will a minor response make the operation significantly less difficult (eg more easily achieving negative margins, avoid a critical vein, or lessen likelihood of conversion of laparoscopic resection)?
Recommendations based on available evidence

• Surgery upfront followed by adjuvant chemotherapy

• If need be, limit chemotherapy to 2-4 cycles before performing surgery

• Avoid pre-operative chemotherapy altogether in cases of small limited lesions (<3cm), else use fiduciary or consider ablation of small lesions pre-chemotherapy
Pattern of recurrence following hepatectomy

- Most patients with multiple, bilobar disease will ultimately recur

- Half will recur within 3 years, half of these recurrences isolated to the liver

- Extra-hepatic metastases most common form of disease recurrence among patients with multiple metastases, liver recurrence most common in patients with small number of mets

- More extrahepatic than intrahepatic recurrence for initially unresectable metastases downstaged by chemotherapy
Repeat hepatectomy for recurrent colorectal metastases

D. A. Wicherts¹, R. J. de Haas¹, C. Salloum¹, P. Andreani¹, G. Pascal¹, D. Sotirop¹, R. Adam¹,²,³, D. Castaing¹,²,³ and D. Azoulay¹,⁴

¹Department of Surgery, Assistance Publique – Hôpitaux de Paris (AP-HP) Hôpital Paul Brousse, Centre Hépatobiliaire, ²Institut National de la Santé et de la Recherche Médicale (INSERM), Unit 785, ³Unité Mixte de Recherche en Santé 785, Université Paris-Sud, and ⁴INSERM, Unit 1004, Villejuif, France

Resections for CLM at Paul Brousse Hospital (1990–2010) 
- n = 1036 patients
- n = 1454 hepatectomies

Patients with two-stage hepatectomy excluded n = 103

Remaining study population 
- n = 933 patients
- n = 1295 hepatectomies

Single hepatectomy 
- n = 645 patients

Repeat hepatectomies 
- n = 288 patients

- 2 hepatectomies 
  - n = 225 patients (78.1%)
- 3 hepatectomies 
  - n = 52 patients (18.1%)
- 4 hepatectomies 
  - n = 11 patients (3.8%)

Total = 650 hepatectomies

BJS 2013
Repeat hepatectomy – Tumour characteristics

Wicherts et al. BJS 2013

<table>
<thead>
<tr>
<th>Liver metastases at diagnosis</th>
<th>First hepatectomy (n = 268)</th>
<th>Second hepatectomy (n = 268)</th>
<th>Third hepatectomy (n = 63)</th>
<th>Fourth hepatectomy (n = 11)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean(s.d.) no. of CLM</td>
<td>3(3)</td>
<td>2(2)</td>
<td>2(2)</td>
<td>2(2)</td>
<td>&lt; 0.001†</td>
</tr>
<tr>
<td>No. of CLM categorized</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>1</td>
<td>75 (28.0)</td>
<td>136 (51.7)</td>
<td>32 (51)</td>
<td>6 (60)</td>
<td></td>
</tr>
<tr>
<td>2–3</td>
<td>84 (32.1)</td>
<td>82 (31.2)</td>
<td>27 (43)</td>
<td>3 (30)</td>
<td></td>
</tr>
<tr>
<td>&gt; 3</td>
<td>59 (36.9)</td>
<td>45 (17.1)</td>
<td>4 (6)</td>
<td>1 (15)</td>
<td></td>
</tr>
<tr>
<td>Maximum size (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>103 (44.2)</td>
<td>139 (62.1)</td>
<td>38 (70)</td>
<td>4 (57)</td>
<td></td>
</tr>
<tr>
<td>≥ 30</td>
<td>130 (55.8)</td>
<td>85 (37.9)</td>
<td>16 (30)</td>
<td>3 (43)</td>
<td></td>
</tr>
<tr>
<td>Bilobar distribution</td>
<td>145 (50.3)</td>
<td>60 (20.8)</td>
<td>7 (11)</td>
<td>0 (0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Initial unresectability</td>
<td>114 (39.6)</td>
<td>42 (14.6)</td>
<td>8 (13)</td>
<td>0 (0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cause of unresectability</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.136</td>
</tr>
<tr>
<td>Multinodular</td>
<td>59 (51.8)</td>
<td>15 (36)</td>
<td>0 (0)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Large size</td>
<td>32 (28.1)</td>
<td>15 (36)</td>
<td>5 (63)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Close vascular relation</td>
<td>17 (14.9)</td>
<td>10 (24)</td>
<td>3 (37)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Extrahepatic disease</td>
<td>6 (5.3)</td>
<td>2 (5)</td>
<td>0 (0)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Concomitant extrahepatic disease</td>
<td>47 (16.3)</td>
<td>33 (11.5)</td>
<td>5 (8)</td>
<td>0 (0)</td>
<td>0.092</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.288</td>
</tr>
<tr>
<td>Lung</td>
<td>16</td>
<td>16</td>
<td>0</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Lymph node</td>
<td>11</td>
<td>6</td>
<td>2</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>20</td>
<td>11</td>
<td>3</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Resection</td>
<td>33</td>
<td>17</td>
<td>5</td>
<td>–</td>
<td>0.043</td>
</tr>
<tr>
<td>Preoperative chemotherapy</td>
<td>218 (75.7)</td>
<td>162 (66.3)</td>
<td>31 (49)</td>
<td>5 (45)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No. of lines</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.020</td>
</tr>
<tr>
<td>1</td>
<td>149 (56.3)</td>
<td>129 (79.6)</td>
<td>25 (81)</td>
<td>3 (60)</td>
<td></td>
</tr>
<tr>
<td>&gt; 1</td>
<td>69 (31.7)</td>
<td>33 (20.4)</td>
<td>6 (19)</td>
<td>2 (40)</td>
<td></td>
</tr>
</tbody>
</table>
## Repeat hepatectomy - Histopathology

Wichert et al. BJS 2013

<table>
<thead>
<tr>
<th>Time interval between operations (months)*</th>
<th>First hepatectomy (n = 288)</th>
<th>Second hepatectomy (n = 288)</th>
<th>Third hepatectomy (n = 63)</th>
<th>Fourth hepatectomy (n = 11)</th>
<th>P§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colectomy to first hepatectomy</td>
<td>13 (0–113)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>First to second hepatectomy</td>
<td>–</td>
<td>18 (5–146)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Second to third hepatectomy</td>
<td>–</td>
<td>–</td>
<td>16 (6–59)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Third to fourth hepatectomy</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>21 (4–103)</td>
<td>–</td>
</tr>
<tr>
<td>No. of metastases detected</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>72 (27.8)</td>
<td>118 (47.0)</td>
<td>17 (61)</td>
<td>2 (67)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>2–3</td>
<td>93 (35.9)</td>
<td>94 (37.5)</td>
<td>11 (39)</td>
<td>1 (33)</td>
<td></td>
</tr>
<tr>
<td>&gt; 3</td>
<td>94 (36.3)</td>
<td>39 (15.5)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0.364</td>
</tr>
<tr>
<td>PVE</td>
<td>15 (5.2)</td>
<td>6 (2.1)</td>
<td>2 (3)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Major resection (≥ 3 segments)</td>
<td>97 (33.7)</td>
<td>49 (17.0)</td>
<td>3 (5)</td>
<td>1 (9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Type of resection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anatomical</td>
<td>89 (31.0)</td>
<td>74 (27.9)</td>
<td>14 (23)</td>
<td>1 (9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Non-anatomical</td>
<td>96 (34.1)</td>
<td>138 (52.1)</td>
<td>42 (68)</td>
<td>9 (82)</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>100 (34.8)</td>
<td>53 (20.0)</td>
<td>6 (10)</td>
<td>1 (9)</td>
<td></td>
</tr>
<tr>
<td>Vascular occlusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>None</td>
<td>77 (33.5)</td>
<td>36 (16.0)</td>
<td>6 (21)</td>
<td>9 (82)</td>
<td></td>
</tr>
<tr>
<td>Selective</td>
<td>16 (7.0)</td>
<td>8 (3.6)</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Total particular</td>
<td>116 (50.4)</td>
<td>166 (73.8)</td>
<td>16 (57)</td>
<td>1 (9)</td>
<td></td>
</tr>
</tbody>
</table>
Overall survival  

- Similar postoperative morbidity and mortality
- 3 and 5yr OS: 76% and 54% with repeat hepatectomy, 58% and 45% with one hepatectomy

Wicherts et al. BJS 2013
Survival benefit of repeat resection of successive recurrences after the initial hepatic resection for colorectal liver metastases


- 1996-2010: 336 pts upfront liver resection
- Adjuvant chemotherapy not standard of care; 77 pts receiving chemotherapy excluded
- Surgical management: Upfront resection regardless of number, distribution or extent
Survival benefit of repeat resection of successive recurrences after the initial hepatic resection for colorectal liver metastases.


Overall survival

Recurrence free survival

Number at risk
Initial hepatic resection 263
1st repeat surgery 108
2nd repeat surgery 43
3rd repeat surgery 15

Recurrence-free survival probability

Time (years)
0 1 2 3 4 5

Rec. free group [N=65]
Rec. resectable group [N=108]
Rec. unresectable group [N=90]
Survival benefit of repeat resection of successive recurrences after the initial hepatic resection for colorectal liver metastases.


- At each repeat resection, approx 1/3 recurrence free
- Of those recurred, approx half suitable for further resection
- Survival benefit of repeat resections maintained regardless of number of previous resections
- Sequential repeat resections offer possibility of cure
Outcomes after resection and/or radiofrequency ablation for recurrence after treatment of colorectal liver metastases

J. Hof¹, M. W. J. L. A. E. Wertenbroek¹, P. M. J. G. Peeters¹, J. Widder², E. Sieders¹ and K. P. de Jong¹

Departments of ¹Hepatopancreatobiliary Surgery and Liver Transplantation and ²Radiation Oncology, University Medical Centre Groningen, University of Groningen, Groningen, The Netherlands
Outcomes after resection and/or radiofrequency ablation for recurrence after treatment of colorectal liver metastases

J. Hof\textsuperscript{1}, M. W. J. L. A. E. Wertenbroek\textsuperscript{1}, P. M. J. G. Peeters\textsuperscript{1}, J. Widder\textsuperscript{2}, E. Sieders\textsuperscript{1} and K. P. de Jong\textsuperscript{1}

Departments of \textsuperscript{1}Hepatopancreatobiliary Surgery and Liver Transplantation and \textsuperscript{2}Radiation Oncology, University Medical Centre Groningen, University of Groningen, Groningen, The Netherlands

\begin{itemize}
  \item Overall recurrence rate 83.5\% (152/182) for percutaneous RFA cf 66.6\% (201/302) for liver resection (P<0.001)
  \item Intra-hepatic recurrence 59.9\% in RFA vs 23.9\% in liver resection (P<0.001)
  \item Risk of ablation-site recurrence after RFA 26.9\% (50/186pts, 250 lesions)
  \item 92\% (46/50) of ablation site recurrence treated with curative intent (41 repeat RFA, 5 resection)
\end{itemize}
Outcomes after resection and/or radiofrequency ablation for recurrence after treatment of colorectal liver metastases

J. Hof\textsuperscript{1}, M. W. J. L. A. E. Wertenbroek\textsuperscript{1}, P. M. J. G. Peeters\textsuperscript{1}, J. Widder\textsuperscript{2}, E. Sieders\textsuperscript{1} and K. P. de Jong\textsuperscript{1}

Departments of \textsuperscript{1}Hepatopancreatobiliary Surgery and Liver Transplantation and \textsuperscript{2}Radiation Oncology, University Medical Centre Groningen, University of Groningen, Groningen, The Netherlands

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure}
\caption{Overall survival after first intervention}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure2}
\caption{Overall survival after second intervention}
\end{figure}
Selecting patients for a second hepatectomy for colorectal metastases: A systemic review and meta-analysis.

Luo LX et al. EJSO 2014

- 7226 pts from 27 studies

- Recurrent CRLM mote likely solitary, unilobar and smaller

- Better survival after second hepatectomy in high quality studies

- Predictors of better survival after second hepatectomy: DFI>1yr, solitary met, unilobar, size ≤5cm, lack of EHD and R0 resection
Conclusion – repeat hepatectomy

- Morbidity and mortality similar to first time hepatectomy
- Progression free survival maintained with each hepatectomy
- Possible better survival
- Increasing indication for ablative approaches
Evaluating agreement regarding the resectability of colorectal liver metastases: a national case-based survey of hepatic surgeons.

Mohammad WM et al. HPB 2012

- Investigates contemporary hepatic surgeon perceptions of resectability of CLM
- 10 scenarios ranging from a solitary, peripheral lesion to extensive bilobar involvement
- Evaluate CT images to determine if amenable to resection with or without adjunctive therapies such as radiofrequency ablation, PVE and staged resection
Evaluating agreement regarding the resectability of colorectal liver metastases: a national case-based survey of hepatic surgeons

Mohammad WM et al. HPB 2012

- Consensus only in 2 scenarios with clearly resectable and unresectable disease
- Marked divergence in opinion on the remainder of cases
- Little agreement on type and number of non-resectional adjuncts to surgery
It’s a Fan!

It’s a Spear!

It’s a Snake!

It’s a Wall!

It’s a Tree!

It’s a Rope!

Global Action Plan International

© 2011 Marilyn Mehlmann
Conclusions

• Significant heterogeneity in approaches to patient with CLM
• Lack of randomized trials
• Rapidly changing management paradigms
• Imperative CLM patients to be evaluated in multidisciplinary setting by all surgical and oncologic specialties
Thank You

chan.chung.yip@singhealth.com.sg