The Surgical Management of Colorectal Metastases

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The Basingstoke Hepatobiliary Unit
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Surgical Management of Colorectal Metastases

- The problem in context
- Selection for liver resection
- Strategies to improve operability
- Timing of liver resection
- Extra-hepatic disease
Bowel Cancer Facts

- **Lifetime Risk**
  - Males - 1 in 14
  - Females - 1 in 19
Bowel Cancer Facts

- Despite the rising incidence, survival is also increasing
- 50% Improvement in 10 year survival since 1970s
  - Quality of surgery
  - Quality of staging
  - Improved chemotherapy
  - Better treatment of metastatic disease
Colorectal Liver Metastases

- 15 - 20% present with synchronous metastases\(^1\)
- ~50% will develop liver metastases\(^2\)
- ~30% the liver is the only site of metastatic disease\(^3\)

# CRLM - Natural History

<table>
<thead>
<tr>
<th>% Survival Untreated</th>
<th>1 Year</th>
<th>2 Years</th>
<th>5 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wagner et al 1984</td>
<td>74</td>
<td>42</td>
<td>3</td>
</tr>
<tr>
<td>Strangl et al 1994</td>
<td>46</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>Rougier et al 1995</td>
<td>60</td>
<td>30</td>
<td>3</td>
</tr>
</tbody>
</table>

Median Survival 6 - 9 Months
Few Survive to 5 Years
Resection of CRLM

- 5 Year Survival - 40 - 50%
- 90 Day Mortality - ~1%
CRLM - Improving Survival

- Better Detection
- Better Selection
- Accurate Systemic Staging
- Accurate Liver Specific Staging
- Appropriate Adjunctive Therapies
- Strategies to Improve Resectability
- High Quality Precision Surgery
Detection of Liver Metastases

- Follow-up practice is highly variable - often nihilistic

- **Cochrane Review 2007 (8 Studies)**
  - 5 Yr Survival benefit to intensive F/U
  - Similar number of recurrences, but detected significantly earlier
  - 5 Yr Survival benefit with regular liver imaging
  - Significantly more surgical interventions with curative intent with intensive F/U
Need to intensively Follow-up 12 - 20 Pts to detect 1 “curable” recurrence

Primrose et al 2014
The Importance of Liver Staging

- Extent of Liver Involvement
- Define Anatomy

- Before commencing any adjuvant treatment
  - Disappearing lesions
  - Cystic transformation of lesions
Detailed Pre-treatment Imaging

- Changed stage 56%
- Reduced intra-hepatic recurrence (at diff site) 48 vs 65%
- Reduced rate of re-resection 13 vs 25%

Knowles et al 2012
Biopsy has NO Role for Resectable Lesions

- Biopsy is less sensitive and specific than high quality imaging\(^1\)

- Biopsy reduces matched 5 Yr survival due to seeding\(^2\)

\(^1\)Cresswell et al 2009
\(^2\)Jones et al 2005
Selection - 1999

- Unilobar disease
- <5cm Maximum size
- <4 Metastases
- >1cm Margin
- Absence of Extra-hepatic Disease
- Age
Selection - 1999

- Unilobar disease
- <5cm Maximum size
- <4 Metastases
- >1cm Margin
- Absence of Extra-hepatic Disease
- Age

Only 10% would be resectable
Selection - 2017

- The ability to preserve a sufficient volume of liver parenchyma with adequate inflow and outflow structures
- Complete excision of lesions (1mm margin)\(^1\)
- Liver only disease or the presence of treatable extra-hepatic disease
- General fitness for surgery

\(^1\)Hamady et al 2014
The ability to preserve a sufficient volume of liver parenchyma with adequate inflow and outflow structures

Complete excision of lesions (1mm margin)\(^1\)

Liver only disease or the presence of treatable extra-hepatic disease

General fitness for surgery

>50% Resectable

\(^1\)Hamady et al 2014
Define the Anatomy
Define the Anatomy
Strategies for Improving Resectability

- Neoadjuvant Chemotherapy
- Portal Vein Embolisation
- Staged Resection
- ALPPS Procedure
- Resection & Ablation
- Topical Neo-adj Treatment (Chemo / Radioembolisation)
Conversion Chemotherapy

Neoadjuvant Chemotherapy

16% Inoperable Patients

Liver Resection

39% 5 Yr Survival
Conversion Chemotherapy

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>Surgery Rate (R0)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oxaliplatin-based</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alberts 2003(^{35})</td>
<td>42</td>
<td>36%</td>
</tr>
<tr>
<td>Adam 2004(^{27})</td>
<td>1439</td>
<td>12.5%</td>
</tr>
<tr>
<td>Tournigand 2004(^{45})</td>
<td>111</td>
<td>22%</td>
</tr>
<tr>
<td>Delaunoit 2005(^{36})</td>
<td>267</td>
<td>4%</td>
</tr>
<tr>
<td><strong>Irinotecan-based</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ducreux 2003(^{37})</td>
<td>55</td>
<td>31%</td>
</tr>
<tr>
<td>Pozzo 2004(^{41})</td>
<td>40</td>
<td>33%</td>
</tr>
<tr>
<td>Tournigand 2004(^{45})</td>
<td>109</td>
<td>9%</td>
</tr>
<tr>
<td>Delaunoit 2005(^{36})</td>
<td>264</td>
<td>1%</td>
</tr>
<tr>
<td><strong>Oxiri-based</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Falcone 2004(^{38})</td>
<td>74</td>
<td>26%</td>
</tr>
<tr>
<td>Quenet 2004(^{39})</td>
<td>34</td>
<td>37.5%</td>
</tr>
<tr>
<td>Delaunoit 2005(^{36})</td>
<td>265</td>
<td>4%</td>
</tr>
</tbody>
</table>
Conversion Chemotherapy

Folprecht et al 2005
Effect on Bilobar Disease
Effect on Bilobar Disease
Effect on Large / Poorly Located Disease
Effect on Large / Poorly Located Disease
Chemotherapy Associated Liver Injury

5-FU → Steatosis

Oxaliplatin → Sinusoidal obstruction syndrome

Irinotecan → Steatohepatitis
Chemotherapy Associated Liver Injury

- Increased Infection
- Increased Hepatic Insufficiency
- More Difficult Surgery - Increased Blood Loss

Karoui et al 2006

Majority of effect in 3-4 cycles
Increased morbidity after 5 cycles

Limit duration of Chemotherapy to achieve required effect
Timing of Liver Surgery
Timing of Liver Surgery

- Metachronous Disease
  - Straight to resection
Timing of Liver Surgery

- Inoperable Disease
  - Straight to Conversion Chemotherapy
  - 6 Cycles
  - Re-stage after Cycle 5
Timing of Liver Surgery - Synchronous

❖ Non-critically Located
  ❖ Peri-operative chemotherapy\textsuperscript{1}

❖ Critically Located
  ❖ Straight to surgery
  ❖ Liver before primary\textsuperscript{2}

\textsuperscript{1} In Press 2017
\textsuperscript{2} Welsh et al 2016
Timing of Liver Surgery

❖ Disappearing Lesions
  ❖ Non - Critically Located - Trial of Time off chemo
  ❖ Critically Located - 6 weeks after stopping chemo
Extra-hepatic Metastatic Disease - Dogma

Significance of lymph node involvement at the hepatic hilum in the resection of colorectal liver metastases.
Beckurts KT, Hölscher AH, Thorban S, Rollschweiler E, Stiewert JR.


The role of surgery in the management of pulmonary metastasis.
M J Underwood, T R Graham, and J S Bailey

Influence of metastatic site as an additional predictor for response and outcome in advanced colorectal carcinoma
L Assersohn, A Norman, D Cunningham, T Benepal, PJ Ross and J Oates
Gastrointestinal Unit, The Department of Medicine, Royal Marsden Hospital, Downs Road, Sutton, UK

British Journal of Cancer (1999) 79(11/12), 1800–1805
© 1999 Cancer Research Campaign
Article no. bjoc.1998.0287
Extra-hepatic Metastatic Disease - Dogma

- Improved chemotherapeutic options
- Better understanding of tumour biology
- Safer surgery and better preoperative care
The Basingstoke Ethos

- To offer resection if all tumour sites can be treated (resected / ablated) with acceptable risks of morbidity
Results of R0 Resection for Colorectal Liver Metastases Associated With Extrahepatic Disease

Dominique Elias, MD, PhD, Lucas Sideris, MD, FRCSC, Marc Pocard, MD, PhD, Jean-François Ouellet, MD, FRCSC, Valérie Boige, MD, Philippe Lasser, MD, Jean-Pierre Pignon, MD, PhD, and Michel Duceroux, MD

<table>
<thead>
<tr>
<th>Site of EHD</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peritoneal carcinomatosis</td>
<td>19</td>
</tr>
<tr>
<td>Peritoneal carcinomatosis plus ovary</td>
<td>3</td>
</tr>
<tr>
<td>Hilar lymph nodes</td>
<td>10</td>
</tr>
<tr>
<td>Local recurrences</td>
<td>12</td>
</tr>
<tr>
<td>Retroperitoneal nodes</td>
<td>9</td>
</tr>
<tr>
<td>Lung</td>
<td>10</td>
</tr>
<tr>
<td>Ovary</td>
<td>3</td>
</tr>
<tr>
<td>Abdominal wall</td>
<td>4</td>
</tr>
<tr>
<td>Other sites</td>
<td>5</td>
</tr>
</tbody>
</table>
Concomitant Extrahepatic Disease in Patients With Colorectal Liver Metastases

When Is There a Place for Surgery?

Renè Adam, MD, PhD*†‡, Robbert J. de Haas, MD*†, Dennis A. Wicherts, MD*†, Eric Vibert, MD*, Chadi Salloum, MD*, Daniel Azoulay, MD, PhD*, and Denis Castaing, MD*‡§

<table>
<thead>
<tr>
<th>Patients at risk</th>
<th>Total</th>
<th>1 yr</th>
<th>2 yrs</th>
<th>3 yrs</th>
<th>4 yrs</th>
<th>5 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLM only</td>
<td>654</td>
<td>524</td>
<td>361</td>
<td>237</td>
<td>179</td>
<td>132</td>
</tr>
<tr>
<td>CLM + EHD</td>
<td>186</td>
<td>156</td>
<td>98</td>
<td>54</td>
<td>31</td>
<td>20</td>
</tr>
</tbody>
</table>

\[ P < 0.001 \]
Overall Survival

![Cumulative Survival Graph](image.png)

<table>
<thead>
<tr>
<th>Group</th>
<th>1-yr</th>
<th>2-yr</th>
<th>3-yr</th>
<th>4-yr</th>
<th>5-yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>R0</td>
<td>1102</td>
<td>873</td>
<td>644</td>
<td>467</td>
<td>353</td>
</tr>
<tr>
<td>R2</td>
<td>66</td>
<td>44</td>
<td>20</td>
<td>13</td>
<td>9</td>
</tr>
</tbody>
</table>
Peritoneal Disease

Overall survival of patients who had Cytoreductive Surgery for Colorectal Peritoneal Metastases

<table>
<thead>
<tr>
<th>Group</th>
<th>Median (95% CI)</th>
<th>1-year</th>
<th>3-year</th>
<th>5-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCRS</td>
<td>37.4 months</td>
<td>81.1%</td>
<td>52.2%</td>
<td>42.7%</td>
</tr>
<tr>
<td>MTD</td>
<td>14.2 months</td>
<td>68.1%</td>
<td>8.7%</td>
<td>8.7%</td>
</tr>
</tbody>
</table>
An Approach - “Select the Winners”

- Accurate diagnosis and staging
  - CT / MRI / PET / Laparoscopy
- Assess tumour biology
  - Trial of time
  - Trial of chemotherapy
  - Histology of primary
- Plan treatment for all sites of disease
  - Resection (± HIPEC)
  - Ablation
  - DXT
Take Home Messages

❖ Very few people are “definitely inoperable” - please refer everyone
❖ Get good quality liver imaging “up-front” - this is our road map
❖ NO BIOPSIES - please
❖ Limited extra-hepatic disease is no contra-indication
NHS Patients
linda.hillman@hhft.nhs.uk
01256 313566

Private Patients
amanda.thomas@bmihealthcare.co.uk
01256 377701