Synchronous Colorectal Liver Metastases: The Primary Should be Resected First

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Colorectal Cancer with Hepatic Metastases

- Approximately 20% to 30% will have liver-only metastases on initial evaluation.
- **Synchronous Metastasis**: Definition = within 3 months of diagnosis. (some 6 months).
- Synchronous dz alone is a poor prognostic factor, especially w/ rectal primary.
- **Complete Resection** is associated with 5 Yr Survival ~ 50%.
- Few patients survive with chemotherapy alone

Nordlinger B, Cancer 77:1254-1262, 1996
Leonard et al. JCO 2005;23:2038-48

Competing Problems:
Location, Size & Number

Tumor deposits

Complex problem since surgery for both procedures needs to be scheduled

Question for Debate: Treatment Order
optimal Tx of both the primary and liver

- “Traditional” Approach: Two-stage approach
  1) Colorectal resection (Primary)
  2) F/b chemo and delayed Liver resxn.
- Simultaneous resxn of Primary & CLM
- Liver First (Reverse) Approach: chemo given upfront f/b hepatic resxn and finally colorectal cancer resection

Mentha et al. 2006
Primary First vs Liver First

Data shows that the order doesn’t Matter!

Problems / Pitfalls of Traditional approach

A. Treatment duration can be long (months ~3); risk dz progression in the liver progress beyond resection.

B. Complications from Primary surgery: prevents delivery of systemic chemoRX in ~ 50 %.

Argument for Liver first approach?

A. Prognosis with synchronous disease is driven by the extent of liver metastases.

B. Pre-operative ChemRx is administered in > 80% patients.
   - Improves the intention-to-treat survival since ~ 80% complete treatment.

C. Biology is declared– Extrahepatic disease would preclude resection.
   - Can avoid rectal surgery in patients who progress on chemotherapy.

Resect Primary First

- Primary tumor is large and near-obstructing.
  - Prevents local complications: Obstruction/bleeding.

- Liver First is associated with Dz recurrence ~ 25-67 %

- Survival data is Limited: for the Liver First approach = no difference in outcomes.
Retrospective Studies: Liver-First approach

<table>
<thead>
<tr>
<th>Author</th>
<th>N (Patients)</th>
<th>% 5 yr survival</th>
<th>% Recurrence</th>
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</thead>
<tbody>
<tr>
<td>Brouquet</td>
<td>27</td>
<td>39% (3yr)</td>
<td>46%</td>
</tr>
<tr>
<td>De Jong</td>
<td>22</td>
<td>41% (3yr)</td>
<td>38%</td>
</tr>
<tr>
<td>Mentha</td>
<td>36</td>
<td>31%</td>
<td>70%</td>
</tr>
<tr>
<td>De Rosa</td>
<td>37</td>
<td>30% (3yr)</td>
<td>52%</td>
</tr>
</tbody>
</table>

Broquet et al, J Am Coll Surg 2010; 210:934-941
Mechteld, HPB 2011, 13,745-752
Mentha, Dig Surg 2008;25:430-435
Ayez, Dis Colon Rectum, 2013;56 (3):281-287

Problems with Liver first approach

A. Primary tumor can progress beyond resection
   - Perforation or direct invasion
B. Chemo responsiveness does not always persist.
   - Regrowth of “Disappearing” tumors
   - Regrowth of Primary → Obstruction.
C. Chemotherapy associated toxicity.
D. Disappearing Colorectal Primary.

Categories of Resectability

- Resectable dz by standard approach
- Unresectable but likely convertible with response
- Initially unresectable and unlikely convertible

Extended approach
- Staged resections
- Preop PVE
- Resection plus RFA
- ALPPS
- Hepatic Arterial Infusion Pump
Conclusions

- Hepatic resection remains critical to the long-term outcome of patients with synchronous colorectal metastases.

- These patients are complex and should be managed by multidisciplinary teams:
  - Customized Treatments: individualized and based on extent and location of disease, and tumor biology.
  - Prioritizing Tx should be based on the problematic component of the patient’s dz

Management should be CHEMOTHERAPY-first and not “Liver-first”