H.-R. Raab

Primary with synchronous metastases
Case report Hannover 1991

30 year old man:
Rectal cancer with synchronous
• huge liver metastasis
• infiltration of diaphragm

• rectal extirpation; simultaneous extended right hepatectomy
• postoperative chemotherapy with 5-FU
• died of the disease after 1 year
Strategy in CRC stage IV (liver only)

- R0-resection of both, the primary tumor and the liver metastases offers the only chance of cure!

- Therapeutic strategies
  - in potentially curative situations:
    - increasing resectability
    - lowering the risk for local and systemic recurrence
  - in case of non-curable disease:
    - prolongation of survival
    - improvement of quality of life

No randomized studies!
Strategy in CRC stage IV (liver only)

- treatment in former times?

- is there a benefit from
  - resection of primary tumor?
  - liver resection?

- current strategy?
Traditional Strategy

A palliative excision is the procedure of choice for growths that are still locally removable, and in fact there are few incurable carcinomas of the rectum that cannot be thus excised.

For example, of the last 100 cases with cancer of the rectum seen by me, 95 proceeded to an excision of their growth, in 68 with view to cure, and in 29 purely for palliation.

J.C. Goligher; Surgery of the Anus, Rectum and Colon, Baillière,Tindall & Cassel, London 1967
Strategy in CRC stage IV

- Analysis of Seer-data (Surveillance, Epidemiology and End-Results) USA 1988 – 2000

- Resection of primary tumor
  - in 17,658 of 26,754 patients (CRC Stage IV) = 66%

- Survival
  - colon carcinoma 11 vs. 2 months  p < 0.0001
  - rectal carcinoma 16 vs. 6 months  p < 0.0001

Co-morbidity, extent of metastases, chemotherapy and performance status were not considered!!
Liver-first approach

Outcome of surgery in patients with rectal cancer and simultaneous liver metastases

Overall survival (OS) all groups (n=57)

5 years 38%

Group 1 (n=29)
Primary tumor first
5-year OS 28%

Group 2 (n=8)
Simultaneous resection
5-year OS 73%

Group 3 (n=20)
Liver-first approach
5-year OS 67%
Rational for traditional approach (primary first)

- Treatment of tumor related symptoms
- Prevention of tumor related symptoms
- Primary tumor is source and „motor“ of mets
- Recovery time after resection of primary tumor:
  - „selection period“ (to avoid unnecessary liver resections)

Rational for liver first

- liver metastases determine prognosis
- „better“ condition for RCTx (rectal cancer)
- Recovery time after liver resection:
  - Selection period (to avoid unnecessary colorectal resections)
Stage IV colorectal carcinoma (liver only)
Strategy in Colon carcinoma stage IV (liver only)

Colon carcinoma with synchronous liver metastases

Small asymptomatic carcinoma

- Liver metastases resectable
  - minor liver involvement
    - simultaneous resection
  - major liver involvement
    - CTx; if secondarily resectable
      - simultaneous resection if colon cancer in right colon; two-step with liver first in left colon cancer

Large or symptomatic carcinoma

- Liver metastases primarily not resectable
  - minor liver involvement
    - good PS, Colon-Ca right: simultaneous reduced PS; Colon-Ca left: probably two-step; colon first
  - major liver involvement
    - Colon first; (sometimes only enterostomy)
      - liver resection

- Liver metastases resectable
  - Colon first; sometimes only colostomy
  - CTx; if secondarily resectable
Strategy in rectal carcinoma stage IV (liver only)

rectal carcinoma with synchronous liver metastases

- Small asymptomatic carcinoma
  - Liver metastases resectable
  - Liver metastases primarily not resectable

- Large or symptomatic carcinoma
  - Liver metastases resectable
  - Liver metastases primarily not resectable
Strategy in rectal carcinoma stage IV (liver only)

rectal carcinoma with synchronous liver metastases

Small asymptomatic carcinoma

- Liver metastases resectable
  - minor liver involvement
    - probably simultaneous resection

- Liver metastases primarily not resectable
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Large or symptomatic carcinoma

- Liver metastases resectable
  - CTx

- Liver metastases primarily not resectable
  - Liver first
Strategy in rectal carcinoma stage IV (liver only)

rectal carcinoma with synchronous liver metastases

Small asymptomatic carcinoma
- Liver metastases resectable
  - minor liver involvement
    - probably simultaneous resection
    - CTx; if secondarily resectable
    - Liver first
- major liver involvement
  - CTx

Large or symptomatic carcinoma
- Liver metastases resectable
- Liver metastases primarily not resectable
Liver first - case report

- 51-year-old female patient
- 04/10 diagnosis of non-obstructing adeno-carcinoma of rectosigmoid
- synchronous liver metastases in segments I and IV-VIII
Liver first - case report

29.04.2010  extended right hepatectomy (R0-resection)

01.07.2010  ant. rectal resection with partial adnexectomy right,
            partial peritonectomy in pelvis; loop ileostomy
            pT4a pN2b (11/16) G3 R0

28.07.2010  closure of ileostomy;  adjuvant chemotherapy: FOLFOX
Strategy in rectal carcinoma stage IV (liver only)

rectal carcinoma with synchronous liver metastases

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  - probably simultaneous resection
- Liver metastases primarily not resectable
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CTx; if secondarily resectable
Liver first
Strategy in rectal carcinoma stage IV (liver only)

- **rectal carcinoma with synchronous liver metastases**
  - **Small asymptomatic carcinoma**
    - Liver metastases resectable
    - Liver metastases primarily not resectable
  - **Large or symptomatic carcinoma**
    - Liver metastases resectable
    - Liver metastases primarily not resectable
  - Neoadjuvant RCT
RCTx in rectal carcinoma

- 5-Fu/Oxaliplatin; 50.4 Gy

- undertreatment of liver metastases

- German rectal cancer study:
  - only about 50% of patients received adjuvant therapy after rectal resection

\[ P = .90 \]

improvement of survival by intensifying systemic therapy!
Strategy in rectal carcinoma stage IV (liver only)

rectal carcinoma with synchronous liver metastases

- Small asymptomatic carcinoma
  - Liver metastases resectable
  - Liver metastases primarily not resectable

- Large or symptomatic carcinoma
  - Liver metastases resectable
  - Liver metastases primarily not resectable

Minor liver involvement

- Neoadjuvant CTx; probably stoma/stent
- if secondarily resectable:
  - Liver first

Major liver involvement:

- Neoadjuvante RCT
Case report

- 47 – year-old male
- adenocarcinoma of rectum
- primary tumor circular growth, exophytic; no stenosis
  uT3 uN1; M1 (hep)

**Procedere:**
1. liver resection (bisegmentectomy)
2. RCTx
3. two-stage: resection of rectal cancer
Strategy in rectal carcinoma stage IV (liver only)

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  - Liver metastases primarily not resectable

- Liver metastases resectable
  - minor liver involvement
    - neoadjuvant CTx; probably stoma; two step procedure
      - Liver first
  - major liver involvement
    - Neoadjuvant RCT
      - CTx; probably stoma/stent
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Strategy in rectal carcinoma stage IV (liver only)

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Strategy in rectal carcinoma stage IV (liver only)

rectal carcinoma with synchronous liver metastases

Small asymptomatic carcinoma

Large or symptomatic carcinoma

Liver metastases resectable

Liver metastases primarily not resectable

Liver metastases resectable

Liver metastases primarily not resectable

minor liver involvement

major liver involvement

CTx; falls sekundär resektabel

minor liver involvement

major liver involvement

neoadjuvant CTx; probably stoma/stent; two step procedure

CTx; ggf. Stoma/Stent

if secondarily resectable: Liver first

probably simultaneous resection

CTx

Liver first

Liver first

Liver first

Liver first

Neoadjuvant RCT
Liver first - literature

- retrospective analyses; 2009 -2012, n=37

52% recurrence rate

De Rosa; J Surg Oncol 2013
## Liver first - literature

<table>
<thead>
<tr>
<th>Author/year</th>
<th>patients</th>
<th>rectal/colon</th>
<th>Liver resection n (%)</th>
<th>completed sequence</th>
<th>prognoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mentha / 2008</td>
<td>n = 35</td>
<td>13/17</td>
<td>31 (89%)</td>
<td>30 / 85%</td>
<td>med. survival: 44 months; 1-, 2-, 3-, 4-, 5J-OS resect pat.: 100%, 89%, 66%, 44%, 30%</td>
</tr>
<tr>
<td>Verhoef / 2009</td>
<td>n = 23</td>
<td>23/0</td>
<td>20 (87%)</td>
<td>17 / 73%</td>
<td>Median survival : 19 (7–56) months</td>
</tr>
<tr>
<td>Brouquet / 2010</td>
<td>n = 41</td>
<td>28/13</td>
<td>27 (66%)</td>
<td>27 / 66%</td>
<td>4-year: 52%</td>
</tr>
<tr>
<td>De Jong / 2011</td>
<td>n = 22</td>
<td>19/3</td>
<td>21 (95%)</td>
<td>16 / 73%</td>
<td>3-year.: 41%</td>
</tr>
<tr>
<td>Rosa / 2013</td>
<td>n = 37</td>
<td>25/12</td>
<td>30 (81%)</td>
<td>24 / 65%</td>
<td>1-year-OS: 66% 3-year-OS: 30%</td>
</tr>
<tr>
<td></td>
<td>158</td>
<td>108/45</td>
<td>129 (82%)</td>
<td>114 (72%)</td>
<td></td>
</tr>
</tbody>
</table>

no resection of primary tumor because of „complete response“ n = 5
Liver first - summary

- not enough evidence based data!
- usually CTx first!

- disadvantage:
  - prognoses related factors of primary tumor remain unknown

- advantage:
  - treatment of „prognostic most relevant“ tumor

**Indication for liver first:**

- if there is a risk for irresectability in case of further progression

- if the risk of simultaneous operation is too high

- in case of minor liver involvement but planned RCTx for rectal cancer
There is a **chance of cure** for patients with CRC and synchronous liver metastases.

Treatment is in many cases **multimodal**. The best sequence of therapeutic steps is still unclear.

**Synchronous resection**, if justified in view to the circumstances and the patient's general condition.

**Primary first**, if the risks for liver surgery are high and especially in case of a occurred or threatening complication.

„**Liver first**“ is still experimental! Should be considered in advanced rectal cancer to enable conventional nRCtx.
**Take home message**

- There is a **chance of cure** for patients with CRC and synchronous liver metastases.

- Treatment is in many cases **multimodal**. The optimal sequence of therapeutic steps is still unclear.

- **Synchronous resection**, if justified in view to the circumstances and the patient's general condition.

- **Primary first**, if the risks for liver surgery are high and especially in case of occurred or threatening complication.

- Neoadjuvant Chemotherapy is justified only in unresectable or borderline resectable liver metastases!

- Liver first is still experimental! Should be considered in advanced rectal cancer to enable conventional nRctx.