How to integrate surgery in the treatment of patients with liver-only metastatic disease

Dimitri Dorcaratto MD, PhD, FEBS
Department of Surgery. Liver-Biliary and Pancreatic Unit
Hospital Clínico. University of Valencia
DISCLOSURE

Nothing to disclose
Should we integrate surgery in the treatment of patients with liver-only metastatic disease?
Should we integrate surgery in the treatment of patients with liver-only metastatic disease?
Should we integrate surgery in the treatment of patients with liver-only metastatic disease?
Surgical resection

5-year Survival

10-year Survival

Figure 2 Kaplan-Meier cumulative survival curves of the patients who underwent liver resection (LR) for colorectal cancer (CRC) hepatic metastasis by recurrence-free survival (RFS) and overall survival (OS).

Chan et al. World Journal of Surgical Oncology 2014, 12:155
Tomlinson JS et al. Journal of Clinical Oncology 2007; 25: 4575
Surgical resection offers a substantial chance of cure

**Keys**

- **Primary tumour** *under control*
- **Complete resection (R0)**
- **Liver remnant**
  - Normal liver ≥ 25 %
  - Neoadjuvant Chemo ≥ 30 %
  - Cirrhosis ≥ 40 %
Surgical resection offers a substantial chance of cure

**Keys**

1. Diagnosis and treatment: Multidisciplinary Board
2. Surgical techniques: Anatomy and Technology
3. New strategies and new therapies
MULTIDISCIPLINARY BOARD

- Diagnostic work-up
- Best strategy discussion
- Selection for surgical approach
- Timing for surgery
- Feed-back results
A 10-year study of outcome following hepatic resection for colorectal liver metastases — The effect of evaluation in a multidisciplinary team setting

J.T. Lordan*, N.D. Karanjia, N. Quiney, W.J. Fawcett, T.R. Worthington

The Royal Surrey County Hospital, Guildford, Surrey, GU2 7XX, UK

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DOI 10.1245/s10434-012-2628-4

ORIGINAL ARTICLE – HEPATOBILIARY TUMORS

Colorectal Cancer with Synchronous Resectable Liver Metastases: Monocentric Management in a Hepatobiliary Referral Center Improves Survival Outcomes

Luca Viganò, MD¹, Serena Langella, MD¹, Alessandro Ferrero, MD¹, Nadia Russolillo, MD¹, Elisa Sperti, MD², and Lorenzo Capussotti, MD¹
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% overall survival

% disease-free survival

0.4 Monocentric patients
Early referral
Late referral

0.2

0.0

0.2

0.4

0.6

0.8

1.0

0 1 2 3 4 5

Years

0 1 2 3 4 5

Years
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Ann Surg Oncol
DOI 10.1245/s10434-014-4163-y

Multidisciplinary Cancer Conferences for Gastrointestinal Malignancies Result in Measureable Treatment Changes: A Prospective Study of 149 Consecutive Patients

Jacqueline Oxenberg, DO¹, Wesley Papenfuss, MD¹, Iyare Esemuede, MD¹, Kristopher Attwood, PhD², Marko Simunovic, MD³, Boris Kuvshinoff, MD¹, and Valerie Francescutti, MD¹
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Ann Surg Oncol
DOI 10.1245/s10434-014-4160-y

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Wesley Papenfuss, MD1, Iyare Esemuede, MD1, Kristopher Atwood, PhD2, I. Kuvshinoff, MD1, and Valerie Francescutti, MD1

<table>
<thead>
<tr>
<th>Agreement with initial plan n (%)</th>
<th>No change</th>
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<tbody>
<tr>
<td><strong>Total n (%)</strong></td>
<td>96 (64)</td>
<td>53 (36)</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>81 (91)</td>
<td>16 (33)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Medical oncology</td>
<td>50 (91)</td>
<td>18 (56)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Radiation oncology</td>
<td>16 (94)</td>
<td>4 (25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GI†</td>
<td>2 (100)</td>
<td>1 (33)</td>
<td>0.4</td>
</tr>
<tr>
<td>Radiology</td>
<td>15 (83)</td>
<td>6 (50)</td>
<td>0.10</td>
</tr>
<tr>
<td>Pathology</td>
<td>7 (78)</td>
<td>2 (33)</td>
<td>0.14</td>
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* Gastroenterology/endoscopy
Integrating surgery and oncology

- Preoperative FOLFOX for bad oncological criteria (prognostic).
- Perioperative FOLFOX for good oncological criteria.
- No preoperative therapy (adjuvant?) for excellent oncological criteria.
- Conversion with ‘best systemic therapy’ for difficult surgical criteria (technical).

ESMO GUIDELINES, 2016
Integrating surgery and oncology

- R0 resection achievable
- Liver remnant adequate
Integrating surgery and oncology

- R0 resection achievable
- Liver remnant adequate

- N status of primary
- Disease free interval
- Number of lesions
- Diameter
- CEA
- Extrahepatic disease
- Biology
Goal of preoperative evaluation

Identify potentially resectable patients
**Goal of preoperative evaluation**

Identify **potentially resectable patients**

**Keys**

- **Primary tumour under control**
- **Complete resection (R0)**
- **Liver remnant**
  - Normal liver ≥ 25 %
  - Neoadjuvant Chemo ≥ 30 %
  - Cirrhosis ≥ 40 %
Identify **potentially resectable patients**

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<td>2. Relative</td>
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<tr>
<td>Oncological (B)</td>
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<tr>
<td>1.</td>
<td>Concomitant extrahepatic disease (unresectable)</td>
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<tr>
<td>2.</td>
<td>Number of lesions ≥5</td>
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<tr>
<td>3.</td>
<td>Tumour progression</td>
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Patients should be categorised as A1 or A2/B1, B2 or B3.

<sup>a</sup>All methods, including radiofrequency ablation.
Identify **potentially resectable patients**

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*ESMO GUIDELINES, 2016*
Goal of preoperative evaluation

Identify potentially resectable patients

1. **Define** the number and segmental distribution of LM

2. **Determine** surgical resectability

3. **Identify** extra-hepatic disease
1. **Define** the number and segmental distribution of LM

2. **Determine** surgical resectability

3. **Identify** extra-hepatic disease

*Stepwise imaging approach*

1. Computed tomography

2. Magnetic Resonance Imaging

3. FDG-Positron Emission Tomography
Determine surgical resectability

**PREOPERATORY IMAGING**
- CT-scan
- MRI
- FDG-PET

**INTRAOPERATORY IMAGING**
- INTRA-OPERATIVE ULTRASONOGRAPHY
CT-scan

Contrast enhancement
Arterial and portal phases

CRCLM:
Hypovascular
Rim enhancement washed out
on later phases

Limitations:
Exposure to ionizing radiation
Reactions to iodinated contrast
Sub-centimetre lesions
MRI

- No ionizing radiation
- Higher contrast resolution
- Better for lesions < 1cm
- Better steatosis or changes due to chemotherapy

**CRCLM:**
Hypointense T1
Hyperintense T2
Gadolinium hypovascular enhancement pattern

**Limitations:**
- Availability
- Radiology expertise
- Patient characteristics: claustrophobia, pacemaker...
INTRA-OPERATIVE ULTRASOUND

IOUS + surgical exploration may change the planned surgery up to 20%
Preoperative evaluation and imaging

Surgical eligibility

1. Complete resection of all lesions
2. Free margin resection (R0)
3. Adequate functional liver remnant
4. Fitness for major abdominal surgery
Preoperative evaluation and imaging

Surgical eligibility

1. Complete resection of all lesions
2. Free margin resection (R0)
3. Adequate functional liver remnant
4. Fitness for major abdominal surgery

Liver remnant
- Normal liver ≥ 25 %
- Neoadjuvant Chemo ≥ 30 %
- Cirrhosis ≥ 40 %

Preserved inflow, outflow, biliary drainage
Preoperative evaluation and imaging

Surgical eligibility

1. Complete resection of all lesions

2. Free margin resection (R0)

3. Adequate functional liver remnant

4. Fitness for major abdominal surgery
Clinical Scenarios

Resectable M1 and fit for surgery

Non-resectable M1 but fit for surgery
Conversion surgery after combined therapies

Unresectable M1 or unfit for surgery
Resectable M1 in patients fit for surgery
Surgical technique

ANATOMY

and

TECHNOLOGY
Liver anatomy

Management of colorectal cancer presenting with synchronous liver metastases
Siriwardena AK et al. Nature Reviews Clinical Oncology 2014; 11: 446–459

The Brisbane 2000 terminology of hepatic anatomy and resections.
The terminology committee of the IHPBA.
Retractor Kent / Makuuchii
Intra-operative ultrasonography
CUSA
Argon Beam Coagulator
Tissuelink®
Open approach
Laparoscopic approach
Laparoscopic approach

Laparoscopic Versus Open Resection for Colorectal Liver Metastases

*The OSLO-COMET Randomized Controlled Trial*

Surgical standards

MORBIDITY < 30 %
MORTALITY < 5 %
Non-resectable M1 in patients fit for surgery
Strategies

✓ Neoadjuvant Chemotherapy
✓ Radiofrequency ablation
✓ Portal embolization
✓ Two-stage hepatectomy
✓ Combinations
NEOADJUVANT CHEMOTHERAPY

Conversion is the goal

M₁ UNRESECTABLE

Chemo

M₁ RESECTABLE
NEOADJUVANT CHEMOTHERAPY

Conversion is the goal

M_{1} UNRESECTABLE

M_{1} RESECTABLE

RADIOFREQUENCY ABLATION
RADIOFREQUENCY ABLATION
RADIOFREQUENCY ABLATION
PORTAL EMBOLIZATION

A

B
TWO STAGE HEPATECTOMY

5-Year S
32-64 %
Median survival
24-44 m

Drop-out
35 %

Torzilli G et al. Liver Cancer 2017

± portal embolization
TWO STAGE HEPATECTOMY

Associated liver partition and portal vein ligation for staged hepatectomy (ALPPS)

- Two-stage hepatectomy with very short interval
- Minimizes the drop-out risk
- Extraordinarily rapid hypertrophy of the FRL (10 days)
- Rescue in patients with portal embolization failure

Clearance of the FRL + portal vein ligation + liver parenchyma division

Hepatectomy when the FRL is considered to be large enough
Liver Metastases

Resectables

Prognosis factors*
Low risk

Non-Resectables

Prognosis factors*
High risk

* Nordlinger (96), Fong (99)...Konopke (09)
Number, Size, Lymph node-status, Margin, CEA, Extrahepatic disease, Synchronous...
Liver Metastases

Resectables

- Prognosis factors*
  - Low risk

Non-Resectables

- Prognosis factors*
  - High risk

Surgery + Adjuvant therapy

Prognosis factors*

- Low risk
- High risk

Number, Size, Lymph node-status, Margin, CEA, Extrahepatic disease, Synchronous...

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Liver Metastases

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Liver Metastases

Resectables

- Prognosis factors
  - Low risk

Non-Resectables

- Prognosis factors
  - High risk

Neoadjuvant therapy

- Stable or Responder

Surgery + Adjuvant therapy

Change strategy Chemo

- Progression

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Liver Metastases

* Prognosis factors:
  - Low risk
  - High risk

Resectables

Prognosis factors:

Neoadjuvant therapy

Surgery + Adjuvant therapy

Stable or Responder

Progression

Change strategy Chemo

Palliative

Non-Resectables

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Number, Size, Lymph node-status,
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Liver Metastases

Resectables

Prognosis factors*
Low risk

Neoadjuvant therapy

Stable or Responder

Surgery + Adjuvant therapy

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Change strategy Chemo

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Liver Metastases

Resectables
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Non-Resectables
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Neoadjuvant therapy
- Progression
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  - Progression
  - Palliative

Surgery + Adjuvant therapy

Number, Size, Lymph node-status, Margin, CEA, Extrahepatic disease, Synchronous...

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Liver Metastases

Resectables

- Prognosis factors* Low risk

Non-Resectables

- Prognosis factors* High risk

Neoadjuvant therapy

- Surgery + Adjuvant therapy
  - Stable or Responder
  - Progression

Change strategy Chemo

- Palliative

Surgery + Adjuvant therapy

- Progression

Resectable

- Portal Embolization
  - Radiofrequency
  - Two-stage Hepatectomy

Resectable with combined strategies

Nordlinger (96), Fong (99)...Konopke (09)

Number, Size, Lymph node-status, Margin, CEA, Extrahepatic disease, Synchronous...
Liver Metastases

**Resectables**
- Prognosis factors*
  - Low risk
- Neoadjuvant therapy
  - Stable or Responder
  - Surgery + Adjuvant therapy
  - Neoadjuvant therapy
  - Progression
  - Change strategy Chemo
  - Resectable
  - Portal Embolization
  - Radiofrequency
  - Two-stage Hepatectomy

**Non-Resectables**
- Prognosis factors*
  - High risk
- Neoadjuvant therapy
  - Progression
  - Change strategy Chemo
  - Resectable with combined strategies
  - Surgery + Adjuvant therapy
  - Palliative

* Nordlinger (96), Fong (99)...Konopke (09)
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Liver Metastases

Resectables

- Prognosis factors*
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Non-Resectables

- Prognosis factors*
  - High risk

Neoadjuvant therapy

- Stable or Responder

Surgery + Adjuvant therapy

Change strategy Chemo

Palliative

Progression

Portal Embolization
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Two-stage Hepatectomy

Resectable

- Resectable with combined strategies

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Change strategy Chemo

Nordlinger (96), Fong (99)...Konopke (09)
Number, Size, Lymph node-status, Margin, CEA, Extrahepatic disease, Synchronous...
Summary

Multidisciplinary Treatment
Appropriate selection for the best treatment
Oncological and surgical strategies
Complex surgical techniques in specialized centres
Thank you!!