LAPAROSCOPIC LIVER SURGERY IN COLORECTAL LIVER MEASTASES

Prospective and randomized study comparing open vs laparoscopic liver surgery in colorectal liver metastases

Hospital Universitario Virgen de la Arrixaca Unidad de Cirugía Hepática y Trasplante Hepático
Jefe de Departamento: Prof. P. Parrilla Paricio

Introduction

- **Open surgery is the “gold standard” in liver surgery for colorectal liver metastases because it gets the oncological objectives:**

I. - *Intraoperative objectives:*
   - to achieve correct staging by palpation and ultrasound.
   - to avoid tumor spread.
   - to obtain a good surgical margin.

II. - **Open surgery has a low morbidity and mortality**: mortality is less than 5% and morbidity is between 20 and 30%.

III. - **Open surgery obtains a good 5-year survival**: between 30 and 50%.
Preoperative staging: CT, NMR, PET-CT

Intraoperative staging by laparoscopy:
- PURE LAPAROSCOPIC APPROACH (by Ultrasound)
- HAND-ASSISTED (HAND-ASSISTED + PURE) (by Ultrasound and palpation)
- HYBRID
STAGING BY LAPAROSCOPY

- Staging by HALLS is more complete than pure laparoscopic staging due to:
  - PURE laparoscopic staging is only performed by ultrasound
  - HALLS staging is performed by palpation of the liver and the abdominal cavity and by ultrasound of the liver (small liver metastases in the surface of the liver, peritoneal nodules and hilar lymph nodes could be palpated)

- Furthermore, the adhesions produced by open surgery of the colorectal cancer make more difficult the abdominal exploration by PURE laparoscopy.
There are several publications that show how the laparoscopic exploration of the liver and abdominal cavity in case of PURE Laparoscopic lead to an infrastaging between 10-20%.

These authors, after laparoscopic ultrasound exploration and conversion to open surgery, detect more illness when they add the palpation of the liver and abdominal cavity.
Antonetti et al (Arch Surg, 2003). Hand Assisted laparoscopic liver surgery: (n=15). They convert from Pure lap exploration to “hand assisted”, and in 6 cases (40%) detected more illness

Metcalfe M et al (Arch Surg, 2003) Value laparoscopic staging in CRLM: (n = 24; in Fong et al advanced stages). They convert from Pure lap to open surgery, and in 4 cases there were infrastaging (16%).

Thaler K et al (. 2005) Staging laparoscopy in CRLM: (n = 138). In 18 patients they convert from Pure lap to laparotomy and in 2 case there was infrastaging (11%).

Pilkington SA, et al (HPB, 2007). Laparoscopic staging in CRLM: (n = 77). In 57 patients convert from Pure lap to laparotomy and in 7 (12%) there were infrastaging
A new approach to hand-assisted laparoscopic liver surgery

Ricardo Robles · Caridad Marín · Beatriz Abellán · Asunción López · Patricia Pastor · Pascual Parrilla
• Aim. Open surgery (OS) is currently the “gold standard” for liver metastasis (LM) treatment. However, in order to evaluate the efficiency of laparoscopic surgery (LS) for LM treatment, it is necessary to carry out studies to demonstrate that this technique can obtain the same results as OS. In this study the current position of LS for LM is presented.

• Results. In selected cases for LS, there are similar postoperative morbidity and mortality rates with LS and OS. There are few studies that have shown survival rates at 5 years, although in selected cases, the results of LS and OS are similar.
• In Europe, the laparoscopic liver surgeons prefer the PURE laparoscopic approach (HALLS is used only for conversion)

• Nguyen (Ann Surg 2009), in 103 CRLM, 42 (40.4%) were performed by HALLS, more used in American centers (85%) than in European centers (15%)
**TABLE 8. Survival After Laparoscopic Liver Resection for Colorectal Metastasis to Liver**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>No. Pts</th>
<th>S 1 yr (%)</th>
<th>S 2 yr (%)</th>
<th>S 3 yr (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robles et al</td>
<td>2008</td>
<td>21</td>
<td>100</td>
<td>—</td>
<td>80</td>
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<tr>
<td>Tang et al</td>
<td>2006</td>
<td>4</td>
<td>100</td>
<td>75</td>
<td>—</td>
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<tr>
<td>Vibert et al</td>
<td>2006</td>
<td>41</td>
<td>97</td>
<td>—</td>
<td>87</td>
</tr>
<tr>
<td>O'Rourke</td>
<td>2004</td>
<td>22</td>
<td>—</td>
<td>75</td>
<td>—</td>
</tr>
<tr>
<td>Gigot et al</td>
<td>2002</td>
<td>27</td>
<td>100</td>
<td>100</td>
<td>—</td>
</tr>
</tbody>
</table>
The International Position on Laparoscopic Liver Surgery

The Louisville Statement, 2008

Joseph F. Buell, MD, FACS,* Daniel Cherqui, MD,† David A. Geller, MD,‡ Nicholas O’Rourke, MD,§
David Jamieson, MD,¶ Ibrahim Doganer, MD,|| Alan J. Koffron, MD,** Mark Thomas, MD,**
Brice Gayet, MD,†‡ Ho Siong Han, MD,§§ Go Wakabayashi, MD,¶¶ Giulio Betti, MD,||
Hironori Kaneko, MD,*** Chen-Guo Ker, MD,††† Olivier Scallion, MD,†††‡‡ Alexis Laurent, MD,†
Eddie K. Abdulkh, MD,§§§ Prosanto Chaudhury, MD,§§§§ Erik Dufson, MD,¶¶¶ Clark Gamblin, MD,¶
Michael D’Angelica, MD,**** David Nagerney, MD,***** Giuliano Testa, MD,****** Daniel Labow, MD,%%%%
Derrick Manas, MD,%%%%§§ Ronnie T. Poon, MD,|||| Heidi Nelson, MD,%%%%Robert Martin, MD,*
Bryan Clary, MD,***** Wright C. Pitsen, MD,****** John Martinie, MD,**Jean-Nicolas Vauthay, MD,§§§
Robert Goldstein, MD,§§§§ Susan Rosai, MD,§§§§§ David Barlet, MD,¶¶Joseph Espat, MD,§§§§§
Michael Abecassis, MD,§§§§§ Myrddin Rees, MD,|||| Yuman Fong, MD,*****
Kelly M. McMasters, MD, PhD,* Christoph Brosel, MD,******** Ron Bostil, MD,****
Jacques Belghiti, MD,******** Steven Szeberg, MD,++++++++ and Ravi S. Chari, MD§§§§
Oncologic Results of Laparoscopic Versus Open Hepatectomy for Colorectal Liver Metastases in Two Specialized Centers

Denis Castaing, MD,* † † Eric Vibert, MD,* † † Luana Ricca, MD,* § § Daniel Azoulay, MD, PhD,* Rene Adam, MD, PhD,* and Brice Gayet, MDS§§ (Ann Surg 2009;250: 849–855)

Methods: Two groups composed of 60 patients each were obtained from 2 specialized liver units performing either OH or LH as their primary modality. Cohorts of 215 LH cases and 1783 OH were used to establish the study population. Patients were compared on an intention to treat basis using 9 preoperative prognostic criteria obtained from LiverMetSurvey. These included sex, age, primary tumor localization, number of tumors, diameter of tumor, distribution of metastases, presence of extrahepatic disease, initial respectability, and the use of prehepatectomy chemotherapy. Overall survival and disease-free survival were compared between OH and LH for a follow-up of 36 months.

Results: The median follow-up for the LH group is 30 months and 33 months for the OH group (P = 0.75). One-, 3-, and 5-year patient survival for LH was 97%, 82%, and 64% and 97%, 70%, and 56% in the OH group, respectively (P = 0.32). One-, 3-, and 5-year disease-free survival was 70%, 47%, and 35% and 70%, 40%, and 27% (P = 0.32), respectively for the 2 groups.

Conclusion: In a highly specialized center, first line application of laparoscopic liver resection in selected patients can provide comparable oncologic results to treatment with open liver resection for patients with colorectal liver metastases.
Morioka 2014

- No prospective and randomized study have been performed.
- Only retrospectively case-match control series have been performed, without effects adverse using laparoscopic approach comparing with open surgery:
  - Lower blood losses
  - Lower Hospital Stay
  - Greater surgical time
  - Lower morbidity
  - Similar survival at 3 years.

- OSLO CoMet Trial (http://clinicaltrials.gov/ct2/show/NCT01516710). This trials is testing a number of the comparators evaluated at the consensus conference, but at this time no results are available.
Long-term and perioperative outcomes of laparoscopic versus open liver resection for colorectal liver metastases with propensity score matching: a multi-institutional Japanese study

Toru Beppu · Go Wakabayashi · Kiyoshi Hasegawa · Naoto Gotohda · Toru Mizuguchi · Yutaka Takahashi · Fumitoshi Hirokawa · Nobuhiko Tanai · Manabu Watanabe · Masato Katou · Hiroaki Nagano · Goro Honda · Hideo Baba · Norihiro Kokudo · Masaru Konishi · Koichi Hirata · Masakazu Yamamoto · Kazuhiro Uchiyama · Eiji Uchida · Shinya Kusachi · Kelichi Kubota · Masaki Mori · Keiichi Takahashi · Ken Kikuchi · Hiroaki Miyata · Takeshi Takahara · Masaumi Nakamura · Hironori Kaneko · Hiroki Yamaue · Masaru Miyazaki · Tadahiro Takada

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The author’s affiliations are listed in the Appendix.

Correspondence to:
Toru Beppu, Department of Gastroenterological Surgery, Graduate School of Life Sciences, Kumamoto University, 1-1-1 Honjo, Chuo-ku, Kumamoto 860-8556, Japan.
Email: theppu@kumamoto-u.ac.jp
DOI: 10.1002/jhbp.261

Abstract

Background The aim of the present study was to clarify the surgical outcome and long-term prognosis of laparoscopic liver resection (LLR) compared with conventional open liver resection (OLR) in patients with colorectal liver metastases (CRLM).

Methods A one-to-two propensity score matching (PSM) analysis was applied. Covariates (P < 0.2) used for PSM estimation included preoperative levels of CEA and CA19-9; primary tumor differentiation; primary pathological lymph node metastasis; number, size, location, and distribution of CRLM; existence of extrahepatic metastasis; extent of hepatic resection; total bilirubin and prothrombin activity levels; and preoperative chemotherapy. Perioperative data and long-term survival were compared.

Results From 2005 to 2010, 1,331 patients with hepatic resection for CRLM were enrolled. By PSM, 174 LLR and 342 OLR patients showed similar preoperative clinical characteristics. Median estimated blood loss (163 g vs 415 g, P < 0.001) and median postoperative hospital stay (12 days vs 14 days; P < 0.001) were significantly reduced in the LLR group. Morbidity and mortality were similar. Five-year rates of recurrence-free, overall, and disease-specific survival did not differ significantly. The R0 resection rate was similar.

Conclusions In selected CRLM patients, LLR is strongly associated with lower blood loss and shorter hospital stay and has equivalent long-term survival comparable with OLR.
Minimally Invasive Resection of Colorectal Cancer Liver Metastases Leads to an Earlier Initiation of Chemotherapy Compared to Open Surgery

Samer Tohme¹ · Julie Goswami¹ · Katrina Han¹ · Alexis P. Chidi¹ · David A. Geller¹ · Srinevas Reddy² · Ana Gleisner¹ · Allan Tsung¹

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Abstract

Introduction Previous studies have shown benefit not only from postoperative chemotherapy but also from a short interval to initiation of treatment after resection of primary colorectal cancer. The aim of this study was to determine difference in timing to postoperative chemotherapy for minimally invasive resection (MIR) vs. open resection (OR) of colorectal cancer liver metastases (CRCLM).

Methods This is a retrospective review of 1:1 matched patients undergoing MIR (n=66) and OR (n=66) for CRCLM at a single institution.

Results Patients undergoing MIR of CRCLM had significantly shorter length of hospital stay, fewer major complications, and shorter interval to postoperative chemotherapy (median 42 vs. 63 days, p<0.001). Univariable analysis showed that surgical approach, postoperative complications, blood loss, number of lesions, and length of stay were associated with timing to chemotherapy. On multivariable analysis, surgical approach was still associated with timing to chemotherapy, and postoperative complications resulted in a delay of chemotherapy among patients who underwent OR but not among those who underwent MIR. In addition, worse disease-free survival was seen among patients who received postoperative chemotherapy more than 60 days after surgery.

Conclusion By modifying the deleterious effects of postoperative complications on timing of postoperative chemotherapy, patients undergoing MIR for CRCLM are treated with chemotherapy sooner after surgery compared to those undergoing OR.
Laparoscopic simultaneous resection of colorectal primary tumor and liver metastases: a propensity score matching analysis

Hadrien Tranchart¹² · David Fuks³ · Luca Vigano⁴⁵ · Stefano Ferretti¹² · François Paye⁶ · Go Wakabayashi⁷ · Alessandro Ferrero⁴ · Brice Gayet³ · Ibrahim Daghe¹²

Abstract
Background Preliminary series have shown the feasibility of combined laparoscopic resection of colorectal cancer (CRC) and synchronous colorectal liver metastases (SCRLM). The aim of this study was to compare the short- and long-term outcomes for matched patients undergoing combined resections.

Methods An international multicenter database of 142 patients that underwent combined laparoscopic resection of CRC and SCRLM between 1997 and 2013 was compared to a database of 241 patients treated by open during the same period. Comparison of short- and long-term outcomes was performed after propensity score adjustment.

Results After matching, 89 patients were compared in each group including mostly ASA I–II patients, presenting with mean number of 1.5 CRLM, with a mean diameter of 30 mm, and resectable by a wedge resection or a left lateral sectionectomy. A rectal resection was required in 46 and 43 % of laparoscopic and open procedures, respectively (p = 0.65). There was no difference in global operative time, blood loss and transfusion rates between the two groups. A conversion was required in 7 % of the laparoscopic procedures. Morbidity rates were similar in the two groups (p = 1.0). The 3-year overall survival in the laparoscopy and open groups were 78 and 65 %, respectively (p = 0.17).

Conclusions In patients without severe comorbidities presenting with one, small (≤3 cm), CRLM resectable by a wedge resection or a left lateral sectionectomy, combined laparoscopic resection of CRC and SCRLM allowed similar short- and long-term outcomes compared with the open approach.
Virgen de la Arrixaca Clinic and University Hospital

- Total liver resection: 1256, 857 of them due to CRLM
- We started Laparoscopic Liver Surgery in January 2003
- 169 LR were performed by Laparoscopy in 164 patients (20% of total LR in the same period)
- Median age: 62 years (range 23-85).
APPROACH (n = 169)

- HALLS 122 cases
- PURE 46 cases
- SILLS 1 case
**Indications (n = 169)**

**Benign lesions (n= 30)**
- 14 Haemangiomas
- 4 Focal Nodular Hiperplasia
- 9 Adenomas
- 1 Desmoplastic spindle cell Tumor
- 2 Hydatid cyst

**Malignant tumors (n= 139)**

**Primary (n=33)**
- 23 HCC under cirrhosis
- 8 HCC healthy liver
- 1 Peripheric CC
- 1 Leiomyosarcoma 1º

**Liver Metastasis (n=106)**
- 99 CRLM
- 2 NETLM (+ pancreatectomy)
- 2 GIST
- 2 Breast carcinoma LM
- 1 “tail gut” adenocarcinoma LM
HALLS INDICATIONS (n=122)

Liver metastases (n=106) (99 for CRC, 7 not CRC)

Very large tumors (n=8)

Tumors in right posterior segment (S. VII, VIII) (n=4)

Conversion from PURE laparoscopy (n=4)
HALLS IN CRLM (n=99)

- Cirrhotic liver: 3 cases
- Portal vein embolization: 1 case
- Two-stage liver resection: 4 cases
- Intraoperative radiofrequency: 6 cases
- Simultaneously colon and liver metastases resection: 4 cases
  
  2 Left Hepatectomy, 1 trisegmentectomy V-VI-VII, 1 bisegmentectomy IVB+V

- Hilar lymphadenectomy: 1 case
Results (n= 99)

- Conversion: 1 case
- No intra and postoperative mortality
- Morbidity (IIIb Clavien classification): 6 patients (4.9%)
- Blood losses: median 200 ml.
- Transfusion: 6 patients (4.9%)
- Median surgical time: 120 min (range 20-420)
- Hospital stay: 4 days (2-50)
OBJECTIVE:

- no randomized studies has been carried out to assess the safety and efficacy of laparoscopic liver surgery for colorectal liver metastases.

- Our objective is compare the laparoscopic liver surgery results with the open surgery results in patients with colorectal liver metastases, using a prospective randomized study.
Patients and methods

- We started our laparoscopic liver surgery experience in January 2003, and after the first 50 patients we designed this prospective and randomized study.

- The main end-point was to analyze the 1, 3, and 5 years overall and disease-free survival. Other end-point was to compare the intra and postoperative results. The final study group will be 200 patients, 100 of them in each group.

- The study was started in January 2005. Until now we have included 186 patients in the study (96 operated on by laparoscopy and 90 by open surgery).
Patients and methods

- A preliminary report of the results, until April 2012, was presented in Morioka 2014.

- In this period we performed 339 liver resections for CRLM. Of these, 188 patients were considered unsuitable for laparoscopic surgery because they had advanced disease and were directly treated by laparotomy:

  • Patients with multiple and bilobar LM, huge LM, LM close to big vessels, need for extensive and complex liver resection, re-resections, and two-stage liver resections.

- Of the remaining 151 liver resections, which could be treated laparoscopically, 7 patients were excluded from the study:

  – 3 patients due to liver cirrhosis
  – 4 because they needed a two-stage liver resection
Patients and methods

- Finally 144 patients were randomized in two groups:
  - 72 were operated on by laparoscopy and the others 72 were operated on by open surgery approach.
- The patients with laparoscopic liver surgery were operated on by hand-assissted approach, following of our original technique (Surg. Endosc., 2008)
- Bilateral subcostal laparotomy was the approach used in the open surgery group.
Patients and methods

• Between January 2005-April 2012:

  339 CRLM

  Directly Laparotomy 188

  LM which could be treated laparoscopically 151

  7 patients were excluded

Group of study 144
## Patients and methods

### Selection of patients for the study

<table>
<thead>
<tr>
<th></th>
<th>Randomized patients (n=151)</th>
<th>Advanced stage (n=188)</th>
<th>P=</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative CEA levels</td>
<td>9.7 ± 10.8</td>
<td>132.4 ± 502</td>
<td>0.001</td>
</tr>
<tr>
<td>Number of nodules &gt; 1</td>
<td>45%</td>
<td>70%</td>
<td>0.002</td>
</tr>
<tr>
<td>Number of nodules &gt; 3</td>
<td>19%</td>
<td>33%</td>
<td>0.046</td>
</tr>
<tr>
<td>Bilobar Metastasis</td>
<td>33%</td>
<td>56%</td>
<td>0.005</td>
</tr>
<tr>
<td>Hilar Lymph nodes</td>
<td>3%</td>
<td>9%</td>
<td>0.03</td>
</tr>
<tr>
<td>Number of resected</td>
<td>2</td>
<td>3.5</td>
<td>0.03</td>
</tr>
<tr>
<td>segments</td>
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<td></td>
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</tbody>
</table>
Surgical technique of HALLS
### Surgical technique:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Open (72)</th>
<th>Laparoscopic (72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right hepatectomy</td>
<td>4 cases</td>
<td>4 cases</td>
</tr>
<tr>
<td>Left hepatectomy</td>
<td>4 “</td>
<td>4 “</td>
</tr>
<tr>
<td>Trisegmentectomy</td>
<td>6 “</td>
<td>8 “</td>
</tr>
<tr>
<td>Left lateral sectionectomy</td>
<td>19 “</td>
<td>21 “</td>
</tr>
<tr>
<td>Bisegmentectomy</td>
<td>12 “</td>
<td>9 “</td>
</tr>
<tr>
<td>Segmentectomy</td>
<td>22 “</td>
<td>20 “</td>
</tr>
<tr>
<td>Wedge resections</td>
<td>5 “</td>
<td>6 “</td>
</tr>
</tbody>
</table>
Surgical technique
In the 144 patients of the study we analyzed the following factors:

- **Patients related-factors**: age, gender, comorbidity
- **Primary tumor related-factors**: location, TNM, stage, chemotherapy and/or radiotherapy.
- **Metastasis related-factors**: number, size, location uni-bilobar, synchronous or metachronous presentation, CEA pre and postoperative level.
- **Surgery related-factors**: number of resected segments, intraoperative radiofrequency, surgical time, blood transfusion, surgical margin, Pringle manoeuvre, mortality and morbidity and hospital stay
- **Chemotherapy**: neoadjuvant or adjuvant
- **Liver recurrence of the disease**
- **1, 3 and 5 overall survival and disease free survival**
Follow-up: the results were analyzed at 56 ± 3.75 months
Results

Laparoscopic resection (n=72) vs open surgery (n=72)

- There were no differences between the two groups regarding:
  - Age, gender and comorbidity
  - TNM of the primary tumor
  - Pre and postoperative CEA levels
  - Synchronous and bilobar LM
  - Size and number of LM
  - Intraoperative radiofrequency
  - Major liver resections
  - Number of resected segments
  - Hilar Lymph nodes involved
  - Blood transfusion
  - Surgical margin
  - Adjuvant and neoadjuvant chemotherapy
## Results

Laparoscopic resection (n=72) vs open surgery (n=72)

<table>
<thead>
<tr>
<th></th>
<th>Open Surgery group</th>
<th>Laparoscopic surgery group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pringle manoeuvre</td>
<td>19% (14 cases)</td>
<td>52% (37 cases)</td>
<td>0.01</td>
</tr>
<tr>
<td>Surgical time (min)</td>
<td>125 ± 61</td>
<td>162 ± 78</td>
<td>0.02</td>
</tr>
<tr>
<td>Hospital stay</td>
<td>7 ± 3.5</td>
<td>4 ± 1.4</td>
<td>0.02</td>
</tr>
<tr>
<td>Morbidity</td>
<td>16% (11 cases)</td>
<td>11% (8 cases)</td>
<td>n.s.</td>
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</table>
1, 3 and 5 years overall survival

<table>
<thead>
<tr>
<th></th>
<th>1 year survival</th>
<th>3 years survival</th>
<th>5 years survival</th>
<th>Log-Rank</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open</td>
<td>92%</td>
<td>76%</td>
<td>47%</td>
<td>0.95</td>
<td>n.s.</td>
</tr>
<tr>
<td>Lap</td>
<td>100%</td>
<td>72%</td>
<td>41%</td>
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</table>
Disease Free Survival

<table>
<thead>
<tr>
<th></th>
<th>1 year DFS</th>
<th>3 years DFS</th>
<th>5 years DFS</th>
<th>Log-Rank</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open</td>
<td>82%</td>
<td>53%</td>
<td>33%</td>
<td>1.01</td>
<td>n.s.</td>
</tr>
<tr>
<td>LLS</td>
<td>88%</td>
<td>50%</td>
<td>30%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
• In patients with colorectal liver metastases, using a laparoscopic approach, the Pringle manoeuvre was used more frequently and the surgical time was longer than in open surgery.

• Morbidity and mortality was similar and hospital stay was shorter in the laparoscopic group.

• There were no differences between the two groups regarding Overall Survival and Disease Free Survival.

• More prospective randomized studies are needed to compare open and laparoscopic surgery, which could reproduce our results.