UPDATE ON COLORECTAL LIVER METASTASES

Bjørn Edwin, professor, MD, PhD and Å.A. Fretland, MD for the Oslo-Comet trial group

The Interventional Center and HPB-Department
Oslo University Hospital, Rikshospitalet
Oslo, Norway
We think it would be best if you present the latest results of the RCT CoMet and also address the inherent limitations of lap for CRLM (size, number, location, bilobar, increased risk of missing mets after downstaging chemo) as well as your personal vision on respective indications of lap and open for CRLM. Everybody will be very happy to hear your thoughts on these issues.

Daniel and Oliver
What’s New ....

- More aggressive approach
- Different way to do surgery
  - Laparoscopy
  - Parenchymal sparing surgery
- Local ablation alone or in combination with surgery
- New combinations of neoadjuvant and adjuvant chemotherapy
- New ways to plan surgery
- Future: “Tailor made” or **Personalized cancer treatment**
Multimodal vs. classic approach

"Classical" approach

- Colorectal liver metastases
  - Conventional resection, Formal hepatectomy
  - Repeated resection?
  - Palliative chemotherapy

Multimodal treatment
(more aggressive approach)

- Colorectal liver metastases
  - Neoadjuvant chemotherapy (downstaging)?
    - Portal vein embolisation?
    - Two stage hepatectomy?
      - ALPPS?

- Resection and/or ablation
  - Parenchymal sparing surgery
    - Adjuvant chemotherapy?
      - Lung / adrenal metastases - resection?
        - Re-resection/ablation
          - Chemotherapy
            - Re-evaluation if response

Many more options to be used during the treatment
Different way to do surgery

• Open

• Laparoscopic surgery

• Parenchymal sparing
  – both in open- and laparoscopic surgery.
Parenchyma sparing technique?

Outcomes of parenchyma-preserving hepatectomy and right hepatectomy for solitary small colorectal liver metastasis: A LiverMetSurvey study

Masaru Matsumura, MD, Yoshibito Mine, MD, PhD, Akio Sahira, MD, PhD, Yusuke Insone, MD, PhD, Takeaki Ishizawa, MD, PhD, Hiroshi Ichida, MD, PhD, Ryota Matuki, MD, Masayuki Tamaka, MD, PhD, Yohsiteri Takeo, MD, and Yu Takahashi, MD, PhD

Department of Gastroenterological Surgery, Cancer Institute Hospital, Ariake Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

Conclusions. In patients with advanced CLM, PSH does not increase positive surgical margin or liver recurrence in comparison with MH. A parenchymal-sparing approach offers a high rate of repeat resection for liver recurrence (salvageability).

P = .39. The 5-year recurrence-free survival and overall survival rates were similar in both groups. However, in patients with liver-only recurrence, repeat hepatectomy was more frequently performed in the parenchyma-preserving hepatectomy group than in the right hepatectomy group (67% vs 31%; P < .001), and the overall 5-year survival rate was significantly higher in the parenchyma-preserving hepatectomy group than in the right hepatectomy group (55% vs 23%; P < .001).

Conclusion. Parenchyma-preserving hepatectomy should be considered the standard procedure for solitary small colorectal liver metastasis in the right liver when technically feasible. (Surgery 2017;102:1-13.)
Re-resection --- survival “Worthwhile to do?”
(parenchyma preserving technique - laparoscopic treated - our own results)

(black) – patients WITHOUT LIVER RECURRENT after primary laparoscopic resection (175 patients);

(green) – patients with liver recurrence and ONE LAP RE-RESECTION (84 patients);

(violet) – patients with liver recurrence and TWO LAP RE-RESECTIONS (17 patients);

(red) – patients with liver recurrence and NO SURGICAL TREATMENT (mostly – palliative chemotherapy), 65 patients.

Pure significant difference between group 3 and each of 1, 2 and 4 (p-value <0.001); similar survival for groups 1, 2 and 4.
Vanished Lesions

- Increased use and more effective neoadjuvant/downstaging chemotherapy leads to small lesions disappearing.

- Different solutions/approaches
  - Decrease treatment time or reduce use of neo/adj chemo
  - Treat areas with local ablation and fusion imaging
  - Mark with fusion imaging and resect
  - Anatomical resection
  - "Wait and see"
Inherent limitations of laparoscopy for CRLM (personal opinion)

- Today almost no limitations for laparoscopic surgery in concern of number, location or bilobar lesions.
- “Everything has been done” (reconstruction of vessels and bile duct, ALPPS etc)
- size, relative contraindication

- **Experience and skill dependent**
Local ablation --- reduced numbers of surgical procedures?

- RF, “Nanoknife”, Microwave, HIFU
Personalized cancer treatment based on “omics” data (Genomics, Proteomics Radiomics), including Next-Generation Sequencing (NGS) and Array Comparative Genomic Hybridization (ArrayCGH).
Second International Consensus Meeting in Morioka

Recommendations for Laparoscopic Liver Resection
A Report From the Second International Consensus Conference Held in Morioka

Ann Surg 2015

Results for Comparators in Q1 to Q4 for MINOR LLRs
Recommendation Type A: IDEAL stage 3

Results for Comparators in Q1 to Q4 for MAJOR LLRs
Recommendation Type A: IDEAL stage 2b

| 1 Idea | 2a Development | 2b Exploration | 3 Assessment | 4 Long-term study |
RCT

• "It is always too early until, unfortunately, it’s suddenly too late"

Buxton 1988
RCT  (Beware the learning curve of skill-dependent interventions)

- Multi centre studies with many centres --- comparing different advanced techniques --- may be misleading
  - E.g. Orange II+

The root of all evil...

Alternative: National and International registries
- Effect in real-life settings
Randomized Controlled Trial

Laparoscopic Versus Open Resection for Colorectal Liver Metastases

The OSLO-COMET Randomized Controlled Trial

Åsmund Avdem Freiand, MD,*†‡, Vegar Johansen Dagenborg, MD,§¶†, Guðrun María Waaler Bjørnely, MPhil,*††
Aragaz M. Kazaryan, MD, PhD,* †Ronny Kristiansen,* †Morten Wang Fagerland, MSc, PhD,* †John Hausingen, MD,§§ Tor Inge Tønnessen, MD, PhD,§§§ Andreas Abildgaard, MD, PhD,* †Leonid Borkhvat, MD,* ††† Sheraz Yaqub, MD, PhD,* †Bård I. Røsok, MD, PhD,* †Bjørn Atle Bjørnbeth, MD, PhD,* †Marit Helen Andersen, RN, PhD,* ††† Kjersti Flatmark, MD, PhD,* †§ Eline As, MPhil, PhD,* †† and Bjørn Edwin, MD, PhD,* †† on behalf of the Oslo-CoMet study group

Objective: To perform the first randomized controlled trial to compare laparoscopic and open liver resection.

Summary Background Data: Laparoscopic liver resection is increasingly used for the surgical treatment of liver tumors. However, high-level evidence to conclude that laparoscopic liver resection is superior to open liver resection is lacking.

Methods: Explanatory, assessor-blinded, single-center, randomized superiority trial recruiting patients from Oslo University Hospital, Oslo, Norway from February 2012 to January 2016. A total of 280 patients with resectable liver metastases from colorectal cancer were randomly assigned to undergo laparoscopic (n = 133) or open (n = 147) parenchyma-sparing liver resection. The primary outcome was postoperative complications within 30 days (Acute Physiology grade 2 or higher). Secondary outcomes included cost-effectiveness, postoperative hospital stay, blood loss, operation time, and resection margins.

Results: The postoperative complication rate was 19% in the laparoscopic-surgery group and 31% in the open-surgery group (12 percentage points difference [95% confidence interval 1.67–21.3; P = 0.021]). The postoperative hospital stay was shorter for laparoscopic surgery (53 vs 96 hours, P < 0.001), whereas there were no differences in blood loss, operation time, and resection margins. Mortality at 90 days did not differ significantly from the laparoscopic versus the open surgery (0% vs 0%).
Background

- When the study started our experience was approximately 450 laparoscopic liver operations.
- Up to date we have done almost 1000 (n=992 June 2017) laparoscopic liver operations.
Inclusion criteria

• Parenchyma sparing liver resection for colorectal liver metastases
  – Less than 3 consecutive segments
  – Repeat resections allowed

• Exclusion criteria:
  – Reconstruction of vessels or bile ducts
  – Ablation in addition to resection
Objectives

• Primary objective: 30 days morbidity
  – Yes/No, Accordion Grade II or higher
  – Long list of secondary end points

• Power calculation:
  – OLR: 27% LLR: 13%, 80% strength: n=254
  – 10% drop out: 280 patients planned randomized
Enrolment

- Feb 15th 2012 – Feb 1st 2016
- 308 patients eligible
- 294 patients screened (96%)
Assessed for eligibility (n=294)
- Not meeting inclusion criteria (n=4)
- Declined to participate (n=10)

Randomized (n=280)

Allocated to open liver resection (n=147)
- Received allocated intervention (n=143)
- Did not receive allocated intervention (n=4)
  - Unresectable extrahepatic disease (n=2)
  - Comorbidity (cervical spine fracture) (n=1)
  - Converted to ablation (adhesions) (n=1)

Allocated to lap. liver resection (n=133)
- Received allocated intervention (n=129)
- Did not receive allocated intervention (n=4)
  - Unresectable extrahepatic disease (n=3)
  - Benign tumor (re-evaluated MRI) (n=1)

Follow-Up

Lost to follow-up (n=0)
Discontinued intervention (laparotomy but no resection) (n=5)
  - Unresectable extrahepatic disease (n=5)

Analysed (n=143)
- Excluded from analysis (n=0)

Analysis

Analysed (n=129)
- Excluded from analysis (n=0)
## Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Open Liver Resection</th>
<th>Laparoscopic Liver Resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>65.9</td>
<td>66.7</td>
</tr>
<tr>
<td>Male gender</td>
<td>87 (59%)</td>
<td>77 (58%)</td>
</tr>
<tr>
<td>Body Mass Index (median)</td>
<td>25.3</td>
<td>26.6</td>
</tr>
<tr>
<td>ASA (median)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Number of metastases (mean)</td>
<td>1.6</td>
<td>1.5</td>
</tr>
<tr>
<td>Primary tumor rectum (n, %)</td>
<td>64 (44%)</td>
<td>50 (38%)</td>
</tr>
<tr>
<td>Synchronous metastases (n, %)</td>
<td>91 (62%)</td>
<td>75 (56%)</td>
</tr>
<tr>
<td>Chemotherapy before surgery (n, %)</td>
<td>99 (69 %)</td>
<td>77 (60%)</td>
</tr>
<tr>
<td>Previous liver resection (n, %)</td>
<td>13 (9%)</td>
<td>23 (18%) *</td>
</tr>
<tr>
<td>- Previous open/laparoscopic</td>
<td>10/3</td>
<td>16/7</td>
</tr>
</tbody>
</table>

* = sign. diff.
## Risk scores

<table>
<thead>
<tr>
<th>Risk Score</th>
<th>Open Liver Resection</th>
<th>Laparoscopic Liver Resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical risk score (median)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Basingstoke predictive index</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Iwate complexity score *</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Liver surgery complexity score *</td>
<td>1.36</td>
<td>1.99</td>
</tr>
</tbody>
</table>
# Perioperative results

<table>
<thead>
<tr>
<th></th>
<th>Open Liver Resection</th>
<th>Laparoscopic Liver Resection</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation time (min, median)(95%CI)</td>
<td>120 (106 to 134)</td>
<td>123 (108 to 138)</td>
<td>NS*</td>
</tr>
<tr>
<td>Blood loss (ml, median)(95%CI)</td>
<td>200 (128 to 273)</td>
<td>300 (225 to 375)</td>
<td>0.062*</td>
</tr>
<tr>
<td>Postop hospital stay (hours, median)(95%CI)</td>
<td>96 (90 to 104)</td>
<td>53 (46 to 61)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Involved resection margin (n, %)</td>
<td>10 (7)</td>
<td>8 (6)</td>
<td>NS ^</td>
</tr>
<tr>
<td>Transfusion (patients)</td>
<td>12</td>
<td>10</td>
<td>NS ^</td>
</tr>
<tr>
<td>90-d mortality</td>
<td>1</td>
<td>0*</td>
<td>NS ^</td>
</tr>
</tbody>
</table>

*=median regression, ^=fisher’s mid-p
Primary end point
30-day morbidity $\geq$ Accordion grade 2

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Rate</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open Liver Resection</td>
<td>44 (31%)</td>
<td>0.02*</td>
</tr>
<tr>
<td>Laparoscopic Liver Resection</td>
<td>24 (19%)</td>
<td></td>
</tr>
</tbody>
</table>

*Fisher’s mid-p
Morbidity ≥ Accordion grade 4

<table>
<thead>
<tr>
<th></th>
<th>Open Liver Resection</th>
<th>Laparoscopic Liver Resection</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 (7 %)</td>
<td>4 (3 %)</td>
<td></td>
<td>0.08*</td>
</tr>
</tbody>
</table>

*Fisher’s mid-p
# Comprehensive Complication Index

<table>
<thead>
<tr>
<th></th>
<th>Open Liver Resection</th>
<th>Laparoscopic Liver Resection</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9.3 (6.6 to 12.0)</td>
<td>5.2 (3.1 to 7.3)</td>
<td>0.021 *</td>
</tr>
</tbody>
</table>

*Two-sample t-test*
Subgroup analysis
(postero-superior segments (I, IVa, VII and VIII))

• A total of 136 patients with at least one lesion in the PS segments, were analyzed.

• 62 (49%) in laparoscopic group and 74 (52%) in open group.
Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>OLR (n=74)</th>
<th>LLR (n=62)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>66.3</td>
<td>66.1</td>
</tr>
<tr>
<td>Male gender</td>
<td>48 (65%)</td>
<td>31 (51%)</td>
</tr>
<tr>
<td>Body Mass Index (mean)</td>
<td>25.2</td>
<td>24.7</td>
</tr>
<tr>
<td>ASA (median)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Synchronous metastases (n, %)</td>
<td>49 (66%)</td>
<td>32 (52%)</td>
</tr>
<tr>
<td>Chemotherapy w/ 6 months n, (%)</td>
<td>45 (61%)</td>
<td>28 (45%)</td>
</tr>
<tr>
<td>Previous liver resection, n (%)</td>
<td>9 (12%)</td>
<td>13 (21%)</td>
</tr>
<tr>
<td>- Previous open/laparoscopic</td>
<td>7/2</td>
<td>11/2</td>
</tr>
</tbody>
</table>
### Perioperative results and histopathological data

<table>
<thead>
<tr>
<th></th>
<th>OLR (n=74)</th>
<th>LLR (n=62)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation time, min, mean (range)</td>
<td>143 (28-390)</td>
<td>145 (60-328)</td>
<td>NS</td>
</tr>
<tr>
<td>Blood loss, ml, median (range)</td>
<td>250 (20-2000)</td>
<td>500 (20-3800)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pringle maneuver, n (%)</td>
<td>2 (2.7)</td>
<td>4 (6.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Postop hospital stay, days, median (range)</td>
<td>4 (2-23)</td>
<td>2 (1-29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total number of removed lesions, n, mean (range)</td>
<td>146</td>
<td>111</td>
<td>NS</td>
</tr>
<tr>
<td>Total weight of specimens, gr, median (range)</td>
<td>47 (2-420)</td>
<td>68 (4-375)</td>
<td>0.05</td>
</tr>
<tr>
<td>Involved resection margin, n (%)</td>
<td>7 (9.5)</td>
<td>3 (4.8)</td>
<td>NS</td>
</tr>
</tbody>
</table>
Primary end point

30-day morbidity, Accordion grade ≥ 2

<table>
<thead>
<tr>
<th></th>
<th>OLR (n=74)</th>
<th>LLR (n=62)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 (31%)</td>
<td>16 (26%)</td>
<td>0.49</td>
<td></td>
</tr>
</tbody>
</table>

No 90-day mortality
Comprehensive Complication Index

<table>
<thead>
<tr>
<th>Procedure</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open Liver Resection</td>
<td>NS</td>
</tr>
<tr>
<td>Laparoscopic Liver Resection</td>
<td></td>
</tr>
<tr>
<td>10,1 (6-14)</td>
<td></td>
</tr>
<tr>
<td>6,8 (4 to 10)</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion

• Higher blood loss in laparoscopic group (limitation!). Other perioperative results are similar.

• Similar postoperative complications rate (OLR- 31% vs LLR-25%).

• *Postop. hospital stay was significantly shorter after LLR* (2 vs 4 days).
Cost evaluation
# Economic evaluation - costs

<table>
<thead>
<tr>
<th>Resource</th>
<th>Laparoscopy</th>
<th>Open surgery</th>
<th>Difference (Lap – Open)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personnel/ room</td>
<td>=</td>
<td>=</td>
<td>$55</td>
<td>n.s.</td>
</tr>
<tr>
<td>Disposables</td>
<td>+</td>
<td>-</td>
<td>$655</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital stay</td>
<td>-</td>
<td>+</td>
<td>- $548</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Initial treatment</td>
<td>$15.058</td>
<td>$14.888</td>
<td>- $169</td>
<td>n.s.</td>
</tr>
<tr>
<td>Complications</td>
<td>=</td>
<td>=</td>
<td>$316</td>
<td>n.s.</td>
</tr>
<tr>
<td>1-4 months</td>
<td>=</td>
<td>=</td>
<td>- $363</td>
<td>n.s.</td>
</tr>
<tr>
<td>Sum costs</td>
<td>$19.000</td>
<td>$18.877</td>
<td>- $123</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

p-value estimated using generalized linear models (GLM) with log link and gamma distribution

n.s. = not significant
Quality of Life – SF 36

**Role Physical**
- Laparoscopic
- Open

1 month: p=0.001
4 months: p=0.02

**Bodily Pain**
- Laparoscopic
- Open

1 month: p= 0.008
4 months: p=NS

**Physical Functioning**

1 month: p= NS
4 months: p=NS

**Vitality**

1 month: p=0.023
4 months: p=NS
Economic evaluation - effect

SF 36 transformed to SF 6D

Quality Adjusted Life Years (QALYs)

Health related quality of life

Baseline 1 month 4 months

Time (months)

Laparoscopy (0.243 QALYs) Open surgery (0.230 QALYs)

*** = p < 0.001
**  = p < 0.05
Economic evaluation – cost-effectiveness

Goal: to inform decision makers on the cost per extra effect of a new treatment (laparoscopy) compared to current treatment (open surgery)

All patients
Laparoscopic surgery (LS) was cost-effective with a 67% certainty
Four very expensive patients (grade 5) were observed:
  3 laparoscopic surgery
  1 open surgery group

Four patients excluded
LS was cost-effective with a 100% certainty

Nb! This only shows where the uncertainty in the cost-effectiveness estimate lies!
Conclusion

In the first RCT on lap vs open liver resection:

- 30-day morbidity ≥ grade II was significantly lower after LLR than OLR (19% vs 31%)
- Postop. hospital stay was significantly shorter after LLR than OLR (2 vs 4 days)
- Perioperative results and hospital costs were similar
- QoL was improved
- *Laparoscopic surgery was shown to be cost-effective*
Thank you very much for your attention
Acknowledgements

- Patients!
- Oslo-Comet study group
- ERAS-team
And a last comment

We do have still a lot of unanswered questions about “what’s best treatment” and we are waiting for new RCT’s

but

laparoscopy has come to stay ........

and in high volume centers with advanced laparoscopic skills almost all types of laparoscopic resections can be performed
Behov (for å kunne føre virksomheten videre)

- Flere hoder (unge og sultene) med gastrokirurgisk vinkling knyttet til IVS virksomheten.
- 1 stilling 50-100% plassert på IVS og HPB seksjonen (ferdig Gastrokirurg)
- 1-2 D-stillinger som knyttes både til IVS og HPB seksjonen
- Finne en ekonomisk løsning for lap.stuen i D7
- Robot 😊
Thank you very much for your attention!
Disclosure Statement of Financial Interest

Gudrun Waaler Bjørnelv:

Nothing To Disclose
Economic evaluation
Economic evaluation

Goal: to inform decision makers on the cost per extra effect of a new treatment (laparoscopy) compared to current treatment (open surgery)

\[
\text{ICER} = \frac{\text{cost laparoscopy} - \text{cost open surgery}}{\text{effect laparoscopy} - \text{effect open surgery}} = \frac{\Delta \text{cost}}{\Delta \text{effect}}
\]

- Incremental cost-effectiveness ratio
Economic evaluation

Goal: to inform decision makers on the cost per extra effect of a new treatment (laparoscopy) compared to current treatment (open surgery)

\[
\text{ICER} = \frac{\text{cost laparoscopy} - \text{cost open surgery}}{\text{effect laparoscopy} - \text{effect open surgery}} = \frac{\Delta \text{cost}}{\Delta \text{effect}}
\]

Willingness to pay (WTP) \(\approx\) $95,000
Economic evaluation

Goal: to inform decision makers on the cost per extra effect of a new treatment (laparoscopy) compared to current treatment (open surgery)

\[
\text{ICER} = \frac{\text{cost laparoscopy} - \text{cost open surgery}}{\text{effect laparoscopy} - \text{effect open surgery}} = \frac{\Delta \text{cost}}{\Delta \text{effect}}
\]

Willingness to pay (WTP) \(\approx\) $95,000

Need to measure:
- effect (laparoscopic and open surgery)
- costs (laparoscopic and open surgery)
Morbidity grade 2

<table>
<thead>
<tr>
<th>Medical Event</th>
<th>Open Liver Resection (22)</th>
<th>Laparoscopic Liver Resection (10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial Surgical Site Infection/bleeding</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Deep Surgical Site Infection</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Sepsis, unknown focus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Other (arrythmia, infections)</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>
### Morbidity grade 3

<table>
<thead>
<tr>
<th>Condition</th>
<th>Open Liver Resection (10)</th>
<th>Laparoscopic Liver Resection (10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infected fluid collection</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>GI ulcer</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Pneumothorax (central line)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Pneumothorax (peroperative)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Bile leak - PTC</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
Morbidity grade grade 4 or higher

<table>
<thead>
<tr>
<th></th>
<th>Open Liver Resection (10)</th>
<th>Laparoscopic Liver Resection (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel perforation</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Intraabdominal hematoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Intraabdominal abscess</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Wound dehiscence</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Ileus</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism / ARDS</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
Liver Resections at Oslo University Hospital
February 2012 - January 2016

Hemihepatectomy 329

Parenchyma sparing resections 729

Other malignancy 151
Benign tumors 68
Synchronous ablation 50
Planned as hemihepatectomy 26
Extrahepatic metastases 27

Previously randomized 34
Synchronous resection / HIPEC 23
Vascular reconstruction 21
Liver transplanted (SECA) 4
Planned 2-stage resection 17

No consent 10

Eligible for the trial 308
Not considered 14

Screened 284
Patients

137 patients

Only PS segments
81 patients

Both PS and AL segments
55 patients
Economic evaluation - costs

Initial hospital stay (patient records)

- Patient flow
  - Time in different wards (hours)
  - Discharged to other hospital (days)

- Surgery estimated as a function of time of surgery:
  - Personnel
    - 1 chief of surgery, 1 surgeon in training, 1 anaesthesiologist, 1.5 anaesthesiologic nurses and 2.5 surgical nurses
  - Disposable equipment (micro-costing, n = 100)
  - Operation theatre

- Actual use:
  - Transfusion, extra procedures (e.g. drainage) and imaging.
Economic evaluation - costs

Complications (during the first 30 days):
• Accordion classification of complications/ patient records
  – Extra procedures (initial hospital stay)
  – Re-admission
  – General practitioner

Utilization of health care between 1-4 months:
• Patient questionnaire
  – Inpatient hospital stay
  – Outpatient visits (chemotherapy or other)
  – General practitioner
Beware the learning curve of skill-dependent interventions

- Majeed, Lancet 1996
  - Lap. vs open cholecystectomy
  - Double-blinded RCT

- Basse, Ann Surg 2005
  - Lap vs open colonic resection
  - Double-blinded RCT

- NO DIFFERENCE
- NO DIFFERENCE

Kristoffer Lassen 2013
Sub-study of the Oslo-CoMet trial

**The Oslo-CoMet Trial**
- Open vs Laparoscopic Liver Resection for Colorectal Metastases
- Primary end point: 30 d morbidity (n=280)

- **Study 1**: Inflammatory response
- **Study 2**: Tumor biology
- **Study 3**: Health economy
- **Study 4**: Pain and QoL
- **Study 5**: Imaging
- **Study 6**: Software development
- **Study 7**: Liver resection map - navigation
- **Study 8**: Long term follow up
- **Study 9**: Adhesions

**Participants**
- Fratland Ph.D.
- V. Dagenborg (PhD)
- G. Bjørnelv (PhD)
- V. Cergiia (PhD)
- Kumar (Ph.D., postdoc)
- Palomar (Ph.D.)
- Aghayan (Ph.D)
- Kristiansen (research)
- Kravik, Heidsve, Ringerud (stud.med)
- Fratland (Ph.D.)
- Hausken (research)
Economic evaluation

Goal: to inform decision makers on the cost per extra effect of a new treatment (laparoscopy) compared to current treatment (open surgery)
What is HiPerNav?

HiPerNav is an Innovative Training Network (ITN) funded through a Marie Sklodowska-Curie grant. There will be 14 fully funded and 2 partially funded PhD’s working on the project. The project aims to improve soft tissue navigation through research and development, to improve several bottleneck areas:
Video
Future

- 70 – 80% of the liver surgery will be operated laparoscopically