Adhesion formation after open and laparoscopic resection for colorectal liver metastasis

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UNIVERSITETET I OSLO

03.02.2017

Adhesion formation after laparoscopic and open liver surgery.
A follow-up study from the Oslo Comet trial

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2017

Tittel: Adhesion formation after laparoscopic and open liver surgery

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http://www.duo.uio.no

Trykk: Reprosentralen, Universitetet i Oslo

Abstract

Background

Adhesions are a common adverse effect from surgery and a laparoscopic approach is thought to give fewer adhesions than traditional open abdominal surgery. We designed a retrospective study to compare the severity of adhesion after laparoscopic and open resection of colorectal liver metastases.

Methods

This was a follow-up study of the Oslo-Comet study. Videos obtained during laparoscopic re-resection of liver metastasis from patients previously randomized to open or laparoscopic liver resections were analyzed for time spent on adhesiolysis and severity of adhesions by a blinded researcher. Hospital stay and major complications were then registered and added to the comparison.

Results

12 videos were analyzed. Mean time spent on adhesiolysis was 17,15 minutes in the laparoscopic (n=8) vs 48,15 minutes in the open surgery (n=4) group (p=0,026). Mean Zühlke score was 2,5 and 3,7 in the laparoscopic and open group respectively (p=0,033). No significant differences were found on postoperative hospital stay or major complications.

Discussion

Time spent on adhesiolysis was significantly lower in the group previously randomized to laparoscopic compared to open surgery. Open surgery increased the time spent on adhesiolysis by almost a threefold compared to a laparoscopic approach. The severity of the adhesions measured in Zühlke score was also significantly lower in the laparoscopic group. We did not find any difference in length of hospital stay or distribution and severity of adhesions measured in Peritoneal Adhesion Index (PAI) between the two groups. One person was in the need for repeated surgery due to complications, and one patient had to be converted from laparoscopic to open surgery due to adhesions. The population however is too small to draw any conclusions, and a larger study is needed.

Acknowledgements

Takk til vegleiaren min Åsmund Avdem Fretland for stort tolmod og gode tilbakemeldingar heile vegen.

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Introduction:

Adhesions are bands of scar tissue that may form between the intra abdominal organs. Adhesion formation is a common adverse effect of surgery and it occurs in as much as 90% of all abdominal surgery (1). Adhesions have a variety of consequences, such as small bowel obstruction, female infertility and chronic pain(1, 2). Post-surgery adhesions can account for more than 50% of small bowel obstructions (3). The Surgical and Clinical Adhesion Research (SCAR-3) study indicated a 5% risk of readmission directly related to adhesions after lower abdominal surgery(4, 5). Readmissions with repeated surgery may be complicated by adhesions (6, 7). Adhesiolysis is the surgical removal of adhesions. It is commonly performed when operating on patients who previously have undergone abdominal surgery. Studies have found that adhesiolysis was needed in 89% of patients undergoing repeated median laparotomy (8). Adhesiolysis is associated with an increase in mortality and morbidity, including bowel perforations, sepsis and wound infection (9). Adhesion-related morbidity and complications result in significant costs for the health care system(10, 11). Despite this, Schreinemacher and colleagues found that surgeons underestimate the incidence of adhesions related complications (12).

The pathophysiology of adhesions is not fully understood. Research in both animal and humans suggests a great variety of factors contributing to the formation of peritoneal adhesions(13-15), including both immunological factors and mechanical injuries. Different dissection techniques and type of suture material have shown to influence the adhesion formation(17). The gas composition of the pneumoperitoneum used during laparoscopic surgery might also be of importance(6, 16). The literature is inconclusive regarding the prevention of adhesion formation. Minimizing mechanical injury to the peritoneum and serosal surfaces by applying so-called “good surgical technique" seems to be of importance for adhesion prevention(18). This might lead one to think that laparoscopic surgery is better than open surgery in regards of adhesion formation. The literature however is inconclusive also in this field. Trastulli and colleagues found significant reduction in late intestinal obstruction following laparoscopic rectal resections compared with open resections (22). Some studies show significant differences in adhesion formation at second look, where others could not find any difference in clinically important outcomes such as small bowel obstruction and the ability to become pregnant when comparing open and laparoscopic surgery (2, 16, 18, 19). Laparoscopy does however reduce the risk of adverse effects ant the length of hospital stay in patients undergoing appendectomy and in patients operated for rectal cancer compared with open surgery (20, 21). A laparoscopic approach to abdominal surgery is widely used, and has proven equal to open surgery for a variety of diseases(20-22, 27, 28). So far, no randomized controlled trials have compared open and laparoscopic liver surgery, and The Oslo-CoMet study will be the first to publish data on the subject (29). The data comparing adhesion formation between the to surgical procedures in liver surgery are also scarce.

There is no known method to assess the amount of adhesions other than visual identification during surgery. Thus, the only time the severity and distribution of adhesions in an abdomen can be assessed is during repeated surgery. This means that in order to quantify the amount of adhesions one is dependent on either an external observer or the surgeon to report their findings. Ten Broek et al. showed that the operative notes have low specificity (72,4%) and sensitivity (85,1%), for incidents of adhesions. Furthermore small bowel injuries and other organ injuries were not reported in the operative reports(23). During laparoscopic surgery the surgeon uses live time video from a camera to obtain visual input of the intra abdominal conditions.

The retrospective assessment of the amount of adhesions found during surgery is only possible by viewing these video recordings from the laparoscopic surgery.

There is no standard classification of assessing the severity of adhesions. The Zühlke classification (Table 1) (24) has been used in different studies(8, 9), but it scores only the severity of the adhesions, and does not consider the abdominal location. The peritoneal adhesion index (PAI) (Figure 1) has been proposed as a way to classify the adhesions, both according to severity and anatomical location(25). Neither scoring system have been widely used. Other studies have used the amount of time spent on adhesiolysis during surgery as a measurement of the severity of the adhesions(26).

To our knowledge no randomized controlled trials have been performed to compare the adhesion formation between laparoscopic and open liver surgery. Therefore, the aim of this study was to evaluate level of adhesions and time spent on adhesiolysis at repeated laparoscopic liver resections in patients previously randomized to open or laparoscopic liver resection.

Materials and methods:

The Oslo-CoMet Study was a randomized trial between laparoscopic versus open liver resection of colorectal metastases (NCT01516710). This study is a follow-up study of patients included in the Oslo-CoMet trial. Inclusion criteria for the Oslo CoMet trial were parenchyma-sparing resection of colorectal liver metastases in patients at the Oslo University Hospital, excluding formal hemihepatectomies, resections where reconstruction of vessel/bile duct was needed and resections that needed to be combined with ablation. Patients with non-resectable extra hepatic disease, previous liver ablations, and patients where resection of primary tumour was planned at the same procedure were not included.

Patients and inclusion criteria

For the current study the inclusion criteria were as follows:

1. Participant in the Oslo CoMet trial
2. Former laparoscopic or open surgery for liver metastasis.
3. Recurrence of liver metastasis and eligible for surgery.
4. Repeated laparoscopic surgery for recurrent metastasis.
5. Video available from the repeated laparoscopic surgery

Assessment of adhesions

To assess the amount of adhesions, the researcher viewed videos obtained during the laparoscopic re-resection of liver metastasis. The researcher analyzed the videos based on the following parameters: Severity of adhesions using Zühlke-score (table 1); Severity and localization of adhesions using the PAI (figure 1), and time spent on adhesiolysis.

Per- and postoperative complications and hospital stay.

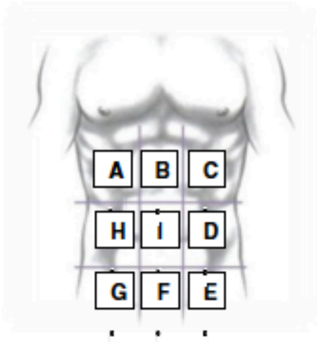
After data collection, the researcher reviewed the patient journals in search for time of post-operative hospital stay and major postoperative complications including the need for repeated surgery, blood transfusions, infections and death. The need for conversion from laparoscopic to open surgery was also noted. The researcher only had access to files from the stay at Oslo University Hospital, Rikshospitalet. Length of stay used in this study is limited to the postoperative course in Rikshospitalet before transfer to smaller local hospitals or other health care institutions.

TABLE 1 Zühlke classification

Zühlke grade	Adhesion description
0	No adhesions
1	Filmy adhesions, easy to separate by blunt dissection
2	Adhesions with beginning vascularisation, blunt and partly sharp dissection needed
3	Adhesiolysis possible by sharp dissection only, clear vascularisation
4	Adhesiolysis possible by sharp dissection only, damage of organ hardly preventable

Zuhlke, Lorenz (24)

PERITONEAL ADHESION INDEX:



Regions:	Adhesion grade:	Adhesion grade score:
A Right upper	____	**0** No adhesions
B Epigastrium	____	**1** Filmy adhesions, blunt dissection
C Left upper	____	**2** Strong adhesions, sharp dissection
D Left flank	____	**3** Very strong vascularized adhesions, sharp dissection, damage hardly preventable
E Left lower	____	
F Pelvis	____	
G Right lower	____	
H Right flank	____	
I Central	____	
L Bowel to bowel	____	

PAI ☐

Figure 1, Peritoneal Adhesion Index, PAI
Coccolini, Ansaloni (25)

Blinding

During the analysis, the researcher was presented with the videos obtained during surgery, without any other information on the patients' age, sex or past surgical history. After this data collection, information about the primary liver resection was matched with the results from the video analysis. The researcher then gained access to the patients' files for investigation of the post-operative course.

Statistical analysis

Statistical analysis were performed in SPSS® for Mac v. 22 (IBM, Armonk, NY). The patients were divided into an open (n=8) and laparoscopic (n=4) based on their primary liver resection. Mean time spent on adhesiolysis and average length of hospital stay was calculated together with mean PAI and Zhülke score in the entire population and in the two subgroups. For measure of variability a 95% confidence interval was used. An independent-samples t-test was conducted to compare time spent on adhesiolysis, PAI- and Zühlke-score and length of postoperative stay in hospital between the groups previously randomized to open and laparoscopic surgery. Differences between the groups were considered statistically significant if the P-value were below 0,05.

Results

After reviewing the follow up database, 35 patients from Oslo-CoMet had repeated laparoscopic surgery for recurrent metastasis. Due to technical difficulties it was not possible to obtain video for 23 of these patients. A total of 13 patients met all the inclusion criteria and was included in this study. One of the patients had to be converted from laparoscopic to open surgery due to severity of adhesions. Data from this patient is used when comparing severity of adhesions, but not for time spent on adhesiolysis, length of hospital stay or other calculations. The mean age of the patients was 62 years, and there were 41% women among the patients.

The mean time spent on adhesiolysis was 37 minutes and the severity of the adhesions was assessed to 3.25 and 9 in Zühlke and PAI score respectively. The mean post-operative hospital stay was 3.5 days.

Time spent on adhesiolysis was significantly lower in the group previously randomized to laparoscopic compared to open surgery (table 3). Open surgery increased the time spent on adhesiolysis by almost a threefold compared to laparoscopic approach (48,15 vs. 17,15 minutes respectively). Only one patient in the open surgery group had a shorter adhesiolysis time than any patient in the laparoscopic group (figure 2). It was not observed any significant differences in length of hospital stay and PAI score between the two groups. The Zühlke score was observed to be significantly lower in the laparoscopic compared to the open group (Table 3).

The distribution of length of hospital stay is demonstrated in figure 3. One patient in the laparoscopic group had a hospital stay of 15 days, otherwise the two groups are quite similar.

No major post-operative complications were noted in the group previously randomized to open surgery (Table 4). However we found the only patient having to be converted from laparoscopic to open surgery due to adhesions in this group. One patient in the laparoscopic group was in need for repeated surgery due to postoperative complications. This patient also had a postoperative infection. Three patients in the laparoscopic group were in need for blood transfusions during the course of the hospital stay (Table 4). No statistical significance was noted between the groups.

Table 2. Baseline characteristics

	Laparoscopic (n = 4)	Open (n = 8)
Age, mean (95% CI)	61 (44 to 79)	63 (51 to 75)
Male gender, n (%)	2 (50%)	5 (62,5%)
Primary laparoscopic colo-rectal cancer surgery	1 (25%)	1 (12,5%)

Table 2 shows the baseline characteristics of the patients included in this study.

Table 3 Difference between the groups				
	Open	Laparoscopic	Difference	p-value
Time spent on adhesiolysis. (95%CI) n=8	2889 (1963 to 3814)	1029 (472 to 1585)	1860 (276 to 3444)	0.026
Zühlke (95% CI) n=9	3.7 (3.2 to 4.2)	2.5 (1.5 to 3.5)	1.17 (0.112 to 2.2)	0.033
PAI (95% CI) n=9	11 (8.4 to 13.8)	5.75 (1.3 to 10.2)	5.361 (-0.013 to 10.7)	0.5
Length of P-O hospital stay n=8	2.4 (1.3 to 3.4)	5.75 (-0.3 to 11.8)	-3.4 (-13 to 6.3)	0.357

Table 3 shows the difference in the variables (Time spent on adhesiolysis, Zühlke score, peritoneal adhesion index (PAI), and length of postoperative (P-O) hospital stay) measured comparing the two surgical approaches.

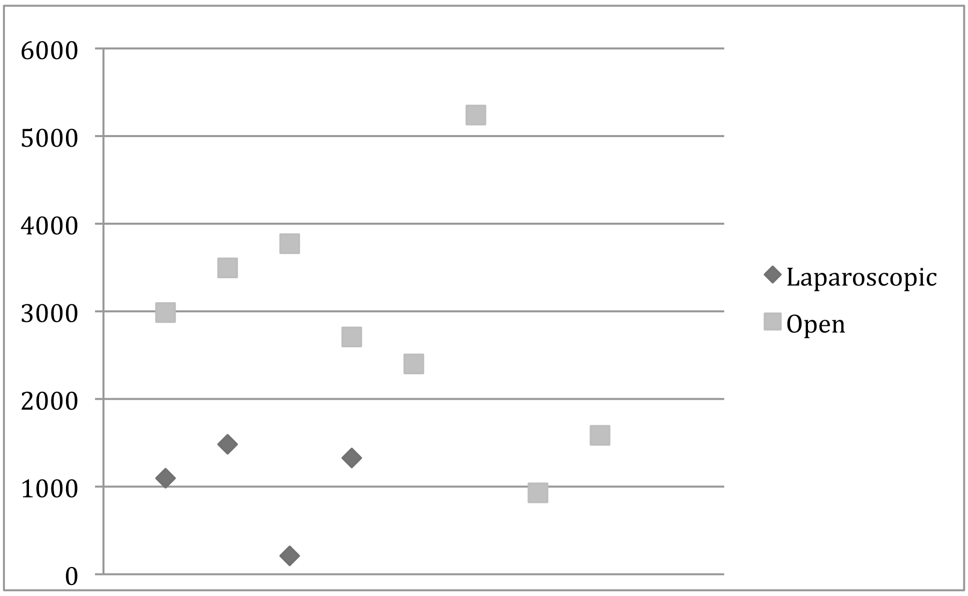


Figure 2 shows the distribution of the time spent on adhesiolysis (in seconds) in the laparoscopic and the open surgery group

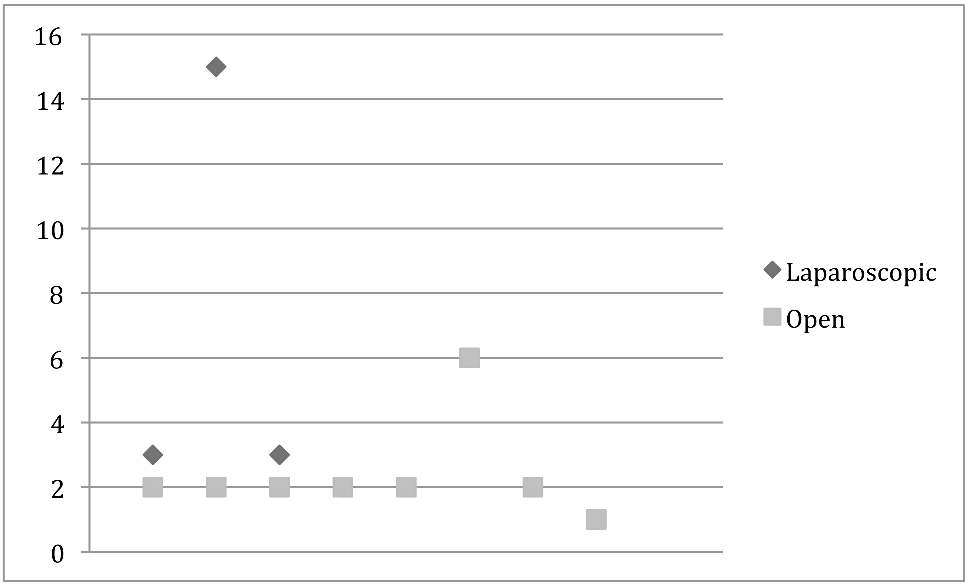


Figure 3 shows distribution of days spent in hospital after surgery before transfer to other hospital

Table 4. Post-operative complications		
	Open group	Laparoscopy
Repeated surgery	0	1
Blood transfusion	0	3
Infection	0	1
Converting to open approach	1	0

Table 5 shows major per- and postoperative complications in the two groups.

Discussion

In this study we compared the level of abdominal adhesions in patients previously operated with either laparoscopic or open liver resection for colorectal metastases. We found that less time was spent on adhesiolysis in the patients who previously had undergone laparoscopic liver resection compared to patients who previously had undergone open liver resection. The severity of the adhesions as measured with Zühlke score was also lower in the laparoscopic group.

There were no significant differences between the two groups when comparing length of hospital stay or distribution of adhesions measured in PAI. One patient in the group previously randomized to laparoscopic had severe postoperative complications (Accordion grade 4 or higher). In the group previously assigned to open surgery, one patient had to be converted from laparoscopic to open surgery.

Previous studies of the problem of postoperative abdominal adhesions are inconclusive but there seems to be a tendency towards less adhesion formation after laparoscopic procedures (18, 30). In a study from 2000, Audebert and co-workers found less adhesions on second-look in patients previously undergoing various laparoscopic procedures compared with conventional surgery.(31) This study supports those findings.

We did find some small differences in the post-operative course of the two groups, but the groups sizes and differences where to small to obtain a statistical significance. This is coherent with the existing literature.

As for the morbidity of adhesions, adhesiolysis during repeated surgery might be of most importance(30). In our study an average of 30 minutes longer time was spent on adhesiolysis in the group previously undergoing open surgery. This supports the previous findings that a laparoscopic approach can make repeated surgery more feasible because of less time spent with adhesiolysis (32).

Recurrence of liver metastasis is up to 70% and surgical resection is the best treatment for this disease (33, 34). Preliminary results from the CoMet trial shows that short-term oncological results are comparable with open surgery for a laparoscopic approach. For these patients a laparoscopic approach might offer a less adherent abdomen, with less time spent on adhesiolysis and possibly less complications during surgery. We might also se the possibility for higher frequency of repeated resections for recurrent liver metastasis.

For academic purposes we would like to point out the use of video obtained during laparoscopic surgery as interesting. By using this method one can possibly reduce the need for real time observations, give a broader group of researchers access to the same material and therefore ease the data collection in this type of studies.

Limitations

There are several limitations to this study, the first being the size of the study population. Even though we have seen some statistically significant differences between the groups, it is not possible to draw conclusions based on the size of this study. Secondly there might be some limitations with the use of video for analysis. As previously stated, a high percentage of eligible patients were excluded because we were not able to retrieve video from the operations. Ideally we should have examined this group and compared demography and mortality to se if our study population is comparable, and hence reduce the risk of possible selection bias. As stated in the introduction the video used for this research is recordings of the live time video used during laparoscopic surgery. Even though it is the same visual input as the surgeon bases the procedure on there is a possibility that minor events occurring during surgery might be missed by the camera and therefore by the surgeon. As for the analysis the severity of the adhesions is based solely on visual input, thus the grading is not based on a skilled surgeons opinion, merely the appearance of the adhesion seen on video. This of course does not tell anything about the texture of the adhesion.

The data on the postoperative course included in this study was limited to the stay at Oslo University Hospital. Due to health care politics in Norway there is a tradition of transferring patients to a local hospital or other health care facility after the patient is deemed stable and in shape for transfer. As the researcher did not have access to the files from the different health care institutions, late complications and differences in actual hospital stay might be missed. Future studies will benefit from having data from the entire postoperative course for the patients.

As for prior abdominal surgeries, this was not taken into consideration in this study. All of the patients had different kinds of colorectal surgery in their medical history. These surgeries were both open and laparoscopic, and could affect the adhesion formation in the whole abdomen.

When considering adhesion formation, “good surgical technique” is thought to be of importance. As all surgeons have slightly different technique, this might make comparison between two patients operated by different surgeons slightly difficult. As for the skill of the surgeon there will of course be differences between the technique applied by an experienced and a not so experienced surgeon. In our study the same team of surgeons operated all the patients with one surgeon doing 9 of the 13 surgeries, which might help making the comparison between patients more accurate.

Conclusion

In this study, we examined the difference of adhesion formation following open and laparoscopic liver resection. We studied time spent on adhesiolysis and severity of adhesions in patients undergoing re-resection of liver metastasis. We also compared the postoperative course of the patients included in this study. As our sample size is small, it is hard to draw conclusions. However, the data presented might be indicative that there is a probable difference between adhesion formation in the group formerly randomized to laparoscopic and open liver surgery. We found that postoperative complications were only limited to the laparoscopic group, but no statistical difference between the groups were noted. Patients with liver metastasis often need repeated resections and there is a possible benefit from less time spent on adhesiolysis and less severe adhesions for these patients. Larger studies are needed to confirm our results, and to explore the potential clinical benefits of a laparoscopic approach to resection of colorectal liver metastases.

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