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Repeated Liver Resection for Colorectal Liver Metastases: A Comparison with Primary Liver Resections concerning Perioperative and Long-Term Outcome

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Introduction. 60% of patients operated for colorectal liver metastases (CRLM) will develop recurrent disease and some may be candidates for a repeated liver resection. The study aimed to evaluate differences in intraoperative blood loss and complications comparing the primary and the repeated liver resection for metastases of colorectal cancer (CRC), as well as to evaluate differences in long-time follow-up. Method. 32 patients underwent 34 repeated liver resections due to recurrence of CRLM and studied retrospectively to identify potential differences between the primary and the repeat resections. Results. There was no 30-day postoperative mortality or postoperative hospital deaths. The median blood loss at repeat resection (1850 mL) was significantly (P = 0.014) higher as compared to the primary liver resection (1000 mL). This did not have any effect on the rate of complications, even though increased bleeding in itself was a risk factor for complications. There were no differences in survival at long-term follow-up. Discussion. A repeated liver resection for CRLM was associated with an increased intraoperative bleeding as compared to the first resection. Possible explanations include presence of adhesions, deranged vascular anatomy, more complicated operations and the effects on the liver by chemotherapy following the first liver resection. 30 out of 32 patients had only one re-resection of the liver.

1. Introduction

The second most common cause of cancer-related deaths worldwide is colorectal cancer (CRC), ranking second in Europe and third in the USA [1].

Surgical resection, if possible, is the standard treatment for patients with a localized tumour, but about 50–75% of patients with CRC will develop colorectal liver metastases (CRLM) [2–7]. Even in patients with advanced CRC disease, the liver may be the sole organ with metastases, which is the case in about 30% of the patients [8, 9]. In these cases, a resection of the CRLM may be potentially curative.

Without treatment, patients diagnosed with CRLM have a median survival time around 8–15 months with a 5-year survival rate of 5% [10–13]. With powerful chemotherapy, the median survival time increases up to as much as two years [14].

1.1. Objective. The aim was to study the difference between the primary and repeated liver resection for CRLM, especially as comes long-term survival, intraoperative bleeding, and rate of complications.

1.2. General Treatment of Colorectal Liver Metastases. Liver resection is, when possible, considered the standard treatment of choice for CRLM. Other types of treatment are methods for local tumour destruction, including radiofrequency ablation. These treatments are most often used in patients with nonresectable liver metastases, but may be used as a part of neoadjuvant and adjuvant treatment, and together with surgical resection in order to improve the results following surgery [15].

The main issue in adjuvant treatment following liver resection concerns chemotherapy. Chemotherapy is otherwise generally palliative in the treatment of metastases
of CRC, but may also prolong the survival time [14]. However, chemotherapy can also be used both as neoadjuvant treatment for downsizing the liver metastases, with our without PVE (portal vein embolization) or other local treatment, making otherwise unresectable tumours surgically respectable. Chemotherapy may also be given as adjuvant treatment following liver resection in order to at least lengthen the period until potential tumor recurrence after the initial liver resection for CRLM happens [16, 17].

1.3. Resection of Colorectal Liver Metastases. The 5-year survival rate after resection of CRLM varies broadly in different reports, ranging between 15–50%, but in more recent studies the range is usually 40–50% [2, 18–21].

20–30% of patients with CRLM directly fulfil criteria which make them suitable for liver resections. The criteria for operating CRLM have changed over time, from looking on what can be removed, to also include optimization of what will remain of the liver. Overall, with all novel treatment options, an increased number of patients with CRLM can be offered the surgical option [2, 22–24].

1.4. Recurrence and Repeat Resection of Colorectal Liver Metastases. Although liver resections are performed with curative intent, 60% will develop recurrent disease. Between 20–30% with recurrence after the first liver resection will have a disease which potentially allows a repeat liver resection. The criteria for surgery are relatively the same as for the initial resection. Survival rates and risk for complications and length of hospital stay are reported similar to that noted after the first resection [15, 25–29].

2. Patients and Methods

Medical data on consecutive patients that underwent liver resection due to colorectal adenocarcinoma metastases at the Department of Surgery, Skåne University Hospital, Sweden, during the period 1995–2009, was collected in a database. The information was taken from patients subjected to liver resection for CRLM. Follow-up data was also retrieved for patients who were referred from other hospitals. Four patients registered as having only local intervention actually had a formal liver resection performed and thus entered the database. The database includes a large variety of information, for example, age, intraoperative bleeding, operation time, and complications.

In total, 240 patients had liver resection due to CRLM during the period 1995–2009. Patients who were included in this study had CRLM and underwent a repeated liver resection during the period 1995–2009 at the Department of Surgery, Skåne University Hospital Lund, Sweden. We identified 32 patients, 30 out of which with one resection of the liver and the other two had two resections, thus making a total of 34 repeated liver resections. All patients were operated upon with curative intent. The 240 primary liver resections served as control group.

2.1. Statistical Methods. The tests used were Mann-Whitney U test, Fisher’s exact test, Kruskal-Wallis test, and the Kaplan-Meier test.

3. Results

There was no 30-day operative mortality or postoperative hospital deaths following the 34 repeat resections. The median age at the primary resection was 66 years compared to 64 at the repeat resection (n.s.). Of the 240 primary resections, 91 were female compared to 14/34 at the repeat resection (n.s.). Of the 240 primary resections served as control group.

There was no difference in the number of patients that received neoadjuvant chemotherapy (within the month prior to the operation) or adjuvant chemotherapy (P = 0.826 and P = 0.748, resp.).

There was no difference in survival (Figure 1) between the two groups (P = 0.556), despite the fact that repeat
was significantly higher in repeated resections as compared to resection well despite a technically di-

resections were less microscopically radical according to the PAD ($P = 0.046$). The tumours were slightly larger at the primary resection, though not significantly ($P = 0.108$).

Increased bleeding at the primary resection (>1000 mL) was associated with a higher risk for both complications ($P = <0.0001$) and an increased length of stay ($P = 0.004$).

A higher ASA-class tended to increase the length of hospital stay ($P = 0.052$). When excluding ASA-class IV from the equation, the difference was not significant ($P = 0.12$). ASA-class did not significantly affect neither bleeding ($P = 0.092$) nor risk for complications ($P = 0.611$; Table 1).

### 4. Discussion

During the last decades, there has been great advancement in the field of management of colorectal liver cancer metastases, including recurrent disease. Repeated resections of the liver for colorectal liver metastases have in most studies proved to be beneficial, even rendering some improvement in cases of recurrent disease. Patients thus tolerated the surgical resection on the natural history, "Indicators of prognosis after hepatic resection for colorectal metastases from colorectal cancer: a systematic review of published studies," *British Journal of Cancer*, vol. 94, no. 7, pp. 982–999, 2006.

We also found that there were no differences between the two groups in terms of how many that received neoadjuvant or adjuvant chemotherapy. This can be interpreted that patients in both groups are treated equally from an oncological point of view and thereby has the same conditions when subjected to liver surgery. Overall, repeat liver resections are handled in a similar way as primary liver resections. By treating the two groups in the same way one can assume that experience accumulated from primary resections are also valid on repeat resections. This is important, as repeat resections are fairly limited in number, though the overall accumulating data support the safety and benefits of repeat liver resections [5, 30–32].

### References


<table>
<thead>
<tr>
<th></th>
<th>Primary resection</th>
<th>Repeat resection</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>66 ± 10 years</td>
<td>64 ± 9 years</td>
<td>n.s.</td>
</tr>
<tr>
<td>Gender</td>
<td>62% males</td>
<td>59% males</td>
<td>n.s.</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1000 ± 1786 mL</td>
<td>1850 ± 1833 mL</td>
<td>0.014</td>
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<tr>
<td>Length of stay</td>
<td>8 ± 8 days</td>
<td>8 ± 3 days</td>
<td>n.s.</td>
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<td>Neoadjuvant chemo. administered</td>
<td>33%</td>
<td>31%</td>
<td>n.s.</td>
</tr>
<tr>
<td>Adjuvant chemo. administered</td>
<td>39%</td>
<td>36%</td>
<td>n.s.</td>
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<td>Clavien grade II+</td>
<td>65%</td>
<td>71%</td>
<td>n.s.</td>
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<td>2-year survival</td>
<td>76%</td>
<td>86%</td>
<td>n.s.</td>
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