Abstract. Background: Curative resection for colorectal cancer and their synchronous liver metastases are increasingly performed. However, it is still unclear whether the operative order affects the surgical outcome in laparoscopic simultaneous resection of primary and liver metastatic lesions. Patients and Methods: A total of 27 patients underwent laparoscopic simultaneous resection of primary colorectal cancer and liver metastases at Kumamoto University Hospital. They were divided into two groups based on the order of resection: Colon-first (n=11) and liver-first (n=16) groups. The surgical outcomes between the two groups were retrospectively compared. Results: There was no significant difference in the perioperative surgical outcomes between the two groups except for operative blood loss, which was significantly less in the liver-first group [164 (range=5-820) versus 560 (range=95-2,016) ml, respectively] (p=0.0299). Conclusion: In the simultaneous resection of primary and liver metastatic lesions, the operative order does not affect the short-term surgical outcomes except for operative blood loss. Colorectal cancer is one of the most common types of cancer. Colorectal liver metastases (CRLMs) are present in 60% of patients with colorectal cancer and 15-20% of patients present CRLM at the time of diagnosis (1, 2). The opportunity to treat synchronous liver metastases (SLMs) is increasing because of the development of improved diagnostic imaging, surgical techniques, and chemotherapy. The presence of SLM is an independent prognostic factor for recurrence and death (3-5). If a SLM is initially unresectable, effective chemo- and targeted therapy may facilitate conversion hepatectomy, resulting in an excellent prognosis (6, 7).

Both simultaneous resection and staged resection of primary and liver metastases in patients with SLM are associated with similar perioperative and oncological outcomes (8). When SLMs are initially non-resectable, chemotherapy is administered first. If they are initially resectable, surgical resection of both primary and metastatic lesions is most effective. Simultaneous resection of primary cancer and liver metastases is increasing because of the advantage of a single operation. Simultaneous resection was considered to increase postoperative complications but recently it was reported that its associated postoperative complications rates were significantly lower (9) or did not differ (10), and the length of hospital stay was also significantly shorter (11). In the simultaneous resection of primary and metastatic lesions, it is still unclear whether the operative order (colon-first or liver-first approach) affects the surgical outcome. Simultaneous laparoscopic resection of primary tumor and liver metastases is said to be technically feasible and safe (12). Laparoscopic surgery was reported to be associated with significantly fewer postoperative complications and was...
cost-effective compared with open surgery (13, 14). Here, we investigated the clinical impact of the operative order (colon-first or liver-first) on short-term surgical outcomes, especially in patients with a laparoscopic approach for both primary and liver metastatic lesions.

**Patients and Methods**

**Patients and study design.** This was a retrospective study of prospectively collected data at Kumamoto University Hospital. Between January 2008 and January 2020, a total of 27 patients underwent simultaneous resection of SLM. The patients were divided into two groups based on the operative order: Colon-first and liver-first groups. Clinicopathological features, operative results, and postoperative complications were compared between the two groups. The use of clinical data was approved by the Institutional Review Board of Kumamoto University Hospital (approval number: 1047) and was carried out in accordance with the Declaration of Helsinki.

**Clinicopathological features and operative methods.** The following data were collected from medical charts: Age, sex, body mass index, American Society of Anesthetists-physical status, primary tumor site (right/left/rectal), primary tumor diameter, number of metastatic liver lesions, number of involved hepatic segments and whether unilobar or bilobar, largest diameter of liver metastases, presence or absence of preoperative chemotherapy, and chemotherapy regimen. The primary tumor site was categorized as the right colon (from the cecum to the transverse colon), the left colon (from the splenic flexure to the sigmoid colon), or rectal colon. The operative order was at the surgeon’s discretion.

**Statistical analysis.** This study’s endpoint was the short-term perioperative results. Clavien–Dindo classification was used to evaluate postoperative complications. All of the statistical analyses were performed with JMP statistical software version 10 (SAS Institute, Inc, Cary, NC, USA). Categorical variables were analyzed using a chi-square test (case number ≥5) or Fisher’s exact test (case number <5), and continuous variables were analyzed by Student’s t-test or Mann–Whitney test. A p-value of less than 0.05 was considered to be significant. Operating room stay time was defined as the time between entry to and exit from the operating room.

**Results**

The baseline characteristics are summarized in Table I. In this cohort, a colon-first procedure was performed for 11 patients, and liver-first for 16 patients. There were no
Table II. Operative methods.

<table>
<thead>
<tr>
<th>Approach</th>
<th>Total (N=27)</th>
<th>Primary first (N=11)</th>
<th>Liver first (N=16)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laparoscopic</td>
<td>27</td>
<td>11</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laparoscopic</td>
<td>27</td>
<td>11</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Hand-assist</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hybrid</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Pure laparoscopic</td>
<td>16</td>
<td>2</td>
<td>14</td>
<td></td>
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<tr>
<td>Colectomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ileocecal resection</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Right hemicolectomy</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Sigmoid colectomy</td>
<td>7</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Left hemicolectomy</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Partial colectomy</td>
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<td>1</td>
<td></td>
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<td>2</td>
<td></td>
</tr>
<tr>
<td>Low anterior resection</td>
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<td>4</td>
<td></td>
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<tr>
<td>Intersphincteric resection</td>
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<td>2</td>
<td></td>
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<tr>
<td>Hepatectomy</td>
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<td></td>
<td></td>
<td>0.81</td>
</tr>
<tr>
<td>Anatomical resection</td>
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<td>2</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Parenchymal resection</td>
<td>17</td>
<td>7</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Pringle maneuver</td>
<td>Yes</td>
<td>18 (66.7%)</td>
<td>8 (72.7%)</td>
<td>10 (62.5%)</td>
</tr>
</tbody>
</table>

The operative methods for primary lesions is shown in Table II. In the liver-first group, pure laparoscopic surgery was performed more often. During hepatectomy, the Pringle maneuver was performed in 18 patients (66.7%). The median amount of blood loss in the liver-first group was smaller than that in the colon-first group [164 (range=5-820) versus 560 (range=95-2,016) ml, p=0.02991] (Table III). On the other hand, there was no significant difference in median operative time, or the operating room stay time between the two groups. Postoperative complications occurred in six patients; however, there was no significant difference in complications of Clavien–Dindo grade of II and III or higher (Table III). There was also no significant difference time to starting a meal after surgery and postoperative hospital stay. There was no patient with re-operation or death within 30 days after surgery.

Discussion

In this study, we elucidated the clinical impact of operative order on short-term surgical outcomes in laparoscopic simultaneous resection for SLM. Operative order did not affect the perioperative outcomes. Interestingly, the liver-first approach provided lower blood loss compared with the colon-first approach in laparoscopic simultaneous resection for SLM. There was no significant difference in the anastomotic leakage rates before and after liver resection in the present study.

The reason for less blood loss in the liver-first group may be due to the restricted volume control during hepatectomy. Low central venous pressure allows easy control of the hepatic veins before and during parenchymal transection (15). These restricted volumes in the liver-first group may have contributed to the reduced blood loss compared with the colon-first group. In addition, the technique and style of laparoscopic liver resection have advanced in the past 12 years. Therefore, this might have affected the outcomes in the the liver-first group in which many pure laparoscopic surgeries were performed.

Although there was no significant difference, the operative time and the operative room stay time for the liver-first group were shorter than in the colon-first group in this study. Regarding these times, particularly in laparoscopic surgery, the positional difference of the patient’s body between primary resection and resection of metastatic lesions during surgery may have been relevant. At our hospital, laparoscopic hepatectomy requires various
Body positions, such as the semi-lateral decubitus position and right upper limb elevation, and use of the intercostal port for individual lesion sites, especially for the right lobe, posterior segment, and subphrenic lesions. The use of an intercostal port and proper management allows for a feasible approach and safe resection during laparoscopic hepatectomy (16). It takes time to adopt such positions without a familiar team, while laparoscopic colectomy requires a normal position such as a supine or lithotomy position. Therefore, performing the hepatectomy first shortens the time required for changing position, which leads to a reduction in the operative time and operating room stay. However, operative times for primary resection and metastatic resection were not measured in this study.

The Pringle maneuver is often performed to control liver inflow during hepatectomy (17, 18), and for reducing blood loss during hepatectomy. However, during simultaneous resection, there are concerns that a lower volume may cause circulatory disorders in organs, and performing the Pringle maneuver may cause intestinal congestion and subsequent anastomotic leakage of the colorectum; however, in the present study, there was no difference in postoperative complication rates between the colon-first and liver-first groups.

This study has some limitations. Firstly, the operative time and blood loss were not evaluated during colectomy and hepatectomy separately. Secondly, the long-term outcome was unclear in the present study. With regard to simultaneous laparoscopic resection for CRLM, it has been reported that the long-term outcomes were similar to those of open surgery (19), whilst the perioperative outcomes were superior (20, 21). Furthermore, it was reported that neither disease-free nor overall survival differed significantly between simultaneous and staged resection for CRLM (22). Finally, this study was a retrospective study. As there were significant differences in the number of liver metastases, the number of affected hepatic segments, and surgical procedures for resection, the number of cases was insufficient to compare two groups with similar backgrounds. It is also possible that the target period was long and the transition to laparoscopic hepatectomy affected the results. Therefore, a large cohort study or a randomized controlled trial is needed to clarify these issues.

**Conclusion**

In the simultaneous resection of primary and liver metastatic lesions, the operative order does not affect the short-term surgical outcomes except for marginally increased operative blood loss in the colon-first approach.

**Conflicts of Interest**

The Authors have no conflicts of interest to declare.
Authors’ Contributions

TT described and designed the article. HH edited the article. HB supervised the editing of the article. The remaining co-authors collected the data and discussed the content of the article. All Authors read and approved the final article.

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