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Short-Term Outcomes of Simultaneous Laparoscopic Colectomy and Hepatectomy for Primary Colorectal Cancer With Synchronous Liver Metastases

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Although simultaneous resection of primary colorectal cancer and synchronous liver metastases is reported to be safe and effective, the feasibility of a laparoscopic approach remains controversial. This study evaluated the safety, feasibility, and short-term outcomes of simultaneous laparoscopic surgery for primary colorectal cancer with synchronous liver metastases. From September 2008 to December 2013, 10 patients underwent simultaneous laparoscopic resection of primary colorectal cancer and synchronous liver metastases with curative intent at our institute. The median operative time was 452 minutes, and the median estimated blood loss was 245 mL. Median times to discharge from the hospital and adjuvant chemotherapy were 13.5 and 44 postoperative days, respectively. Negative resection margins were achieved in all cases, with no postoperative mortality or major morbidity. Simultaneous laparoscopic colectomy and hepatectomy for primary colorectal cancer with synchronous liver metastases appears feasible with low morbidity and favorable outcomes.

Key words: Simultaneous laparoscopic hepatectomy and colectomy – Primary colorectal cancer with synchronous liver metastases – Short-term outcome

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Colorectal cancer (CRC) is a leading cause of cancer-related death globally, and 14.5% of CRC patients have synchronous liver metastases that are identified during the diagnostic workup or during the course of treatment.[1] Surgical resection of the primary CRC and synchronous colorectal liver metastases (SCRLM) is warranted because this strategy offers the most effective therapy and is potentially curative. However, the optimal treatment schedule and strategy for treating CRC with SCRLM with surgery and chemotherapy remains unclear. Several reports have shown the benefit of simultaneous open resection of primary CRC and SCRLM versus a staged approach.[2–4] In addition, recent improvements in laparoscopic surgery for CRC and liver cancer make this option attractive, and there are several reports of simultaneous laparoscopic colectomy and hepatectomy in the literature.[5–14] In spite of these promising developments, though, the feasibility of these procedures has been controversial in terms of efficacy, safety, and outcome. The aim of this study was to evaluate the short-term operative and oncologic outcomes of simultaneous laparoscopic colectomy and hepatectomy for patients with primary CRC and SCRLM.

Materials and Methods

From September 2008 to December 2013, 10 patients underwent simultaneous laparoscopic resection of CRC and SCRLM with curative intent at our institute. All primary tumors and liver metastases were diagnosed preoperatively using contrast-enhanced multi-detector computed tomography and 18F-deoxyfluoroglucose positron emission tomography. Magnetic resonance imaging of the liver metastases was performed as needed. Epidural blocks were used in 3 patients and transversus abdominis plane blocks were used in 2 patients together with general anesthesia. In our current protocol, all patients with resectable CRC with SCRLM were routinely considered for simultaneous laparoscopic resection. Patients with high-risk comorbidities, bulky tumors, extensive lymph node metastases, and cancer invading other organs were excluded. Short-term outcomes were total incision length, operative time, blood loss, postoperative recovery of gastrointestinal function, length of hospital stay, time to start adjuvant chemotherapy, morbidity and mortality within 30 days after surgery, and histopathologic outcomes (including resection completeness; circumferential, proximal, and distal resection margins; and number of retrieved lymph nodes). Complications within 30 days after surgery were categorized using the Clavien-Dindo system.[15] Clinical records and follow-up data for the 10 patients were obtained and analyzed retrospectively.

For the operations, patients were placed in the lithotomy position. A vertical 10- to 30-mm periumbilical incision was made, and a port was placed to create a pneumoperitoneum. Trocar placement was determined according to the location of the tumor using 2–9 operative ports. Liver resectability was always confirmed by intraoperative ultrasonography. The colorectal resection was performed with total laparoscopy according to accepted surgical technique. Specifically, we used a medial to lateral dissection technique that included complete mesocolic excision with central vascular ligation for colon tumors and partial or total mesorectal excision with high ligation of the inferior mesenteric vessels for rectal tumors.[16–20]

For right-sided colon tumors, resection was performed extracorporeally followed by functional end-to-end anastomosis. For left-sided colon or rectal tumors, anastomosis was performed intracorporeally using the double stapling technique. For hepatectomy, laparoscopic partial resection of the liver metastases was performed with 1–4 additional ports or a small incision as necessary. Intermittent Pringle's maneuver and the HALS (hand-assisted laparoscopic surgery) technique were performed in 5 and 2 patients, respectively. A combination of a Cavitron ultrasonic surgical aspirator (CUSA; Cavitron Lasersonic Corp, Stamford, CT), vessel sealing system, and harmonic scalpel was used to divide the parenchyma. Vascular clips were used to divide the hepatic veins as well as the Glissonian pedicles intracorporeally.

Results

Patient characteristics and preoperative diagnoses are summarized in Table 1. There were 2 females and 8 males with a median age of 60 years (range, 52–84), and the median body mass index was 22.4 kg/m^2 (range, 19.0–26.3). The location of the primary CRC was the colon in 6 cases and the rectum in 4 cases. The median number and diameter of the liver metastases were 2 (range, 1–3) and 1.4 cm (range, 0.3–4.7), respectively. In 1 patient, the FOLFOX regimen (infusional 5-fluorouracil and leucovorin + oxaliplatin) and bevacizumab were administered as preoperative chemotherapy.

Table 1 Patient characteristics and preoperative diagnoses

Case	Age/Sex	BMI	Location of colorectal cancer	Location and size of liver metastasis	Preoperative chemotherapy
1	52/F	23.8	Ascending	S6 (4 cm)	-
2	78/M	25.3	Rectum	S7 (2 cm), S8 (1 cm)	-
3	58/M	26.3	Sigmoid	S6 (0.7 cm, 0.3 cm)	-
4	74/M	20.0	Rectum	S3 (1.2 cm), S2 (0.3 cm)	-
5	62/M	21.2	Cecum	S4 (3.5 cm), S8 (1.5 cm)	FOLFOX+Bmab
6	69/M	22.4	Sigmoid	S4/8 (1.5 cm)	-
7	84/M	19.4	Rectum	S4/8 (1.5 cm)	-
8	53/M	19.0	Rectum	S6 (0.9 cm), S7 (1.3 cm, 1.9 cm)	-
9	56/F	23.1	Transverse	S2/3 (4.3 cm), S3 (0.3 cm), S6 (4.7 cm)	-
10	85/M	22.4	Descending	S2 (9.5 mm)	-

BMI, body mass index.

The surgical procedures and outcomes are summarized in Table 2. The first procedures were colectomy in 6 cases and hepatectomy in 4 cases. The surgical procedures for CRC included 2 ileocecal resections, 2 left hemicolectomies, 2 sigmoid resections, 1 high anterior resection, 2 low anterior resections, and 1 intersphincteric resection using a totally laparoscopic approach. Laparoscopic-assisted partial resections of the liver metastases were performed in all patients, including in 2 patients using the HALS approach. The median total incision length and operative time were 10 cm (range, 3–21) and 452 minutes (range, 275–880), respectively. The median estimated blood loss was 245 mL (range, 80–1320) with a need for a blood transfusion in 1 patient. No case was converted to standard open surgery.

The pathologic data and postoperative outcomes are summarized in Table 3. A negative resection margin was achieved in all cases. The median number of retrieved lymph nodes was 19 (range, 10–38). The median times to start oral fluid intake and to make a decision about discharge were 2 postoperative days (range, 2–4) and 13.5 postoperative days (range, 10–18), respectively.

There was no postoperative mortality or morbidity except for 1 patient who was successfully treated with short tube drainage for postoperative ileus (grade 2 on the Clavien-Dindo grade scale) and 1 patient who was treated with antibiotics for surgical site infection (grade 2 on the Clavien-Dindo grade scale).

According to standard treatment, all patients, except for 2 who were 78 and 84 years old, respectively, underwent adjuvant chemotherapy with a median time to therapy of 44 postoperative days (range, 32–67). At a median follow-up of 12 months (range, 2–54), 6 (60%) patients remained recurrence-free, and there was no mortality within 30 days after surgery. In terms of long-term follow-up, one patient died 2 years and 6 months after the operation as a result of primary CRC recurrence.

Discussion

No randomized controlled trials have compared simultaneous versus staged resection of primary

Table 2 Surgical procedures and outcomes

Case	First procedure	Colorectal procedure	Liver procedure	Total incision length (cm)	Operative time (min)	Blood loss (mL)	Transfusion (mL)	R0
1	Liver	IR	PR	10	275	80	-	Yes
2	Liver	HAR	PR	18	467	1320	560	Yes
3	Colorectal	SR	PR	3	355	30	-	Yes
4	Colorectal	LAR	PR	6	567	218	-	Yes
5	Colorectal	IR	PR	5	419	240	-	Yes
6	Liver	SR	PR	15	437	250	-	Yes
7	Liver	LAR	PR	8	749	300	-	Yes
8	Colorectal	ISR	PR (HALS)	21	880	370	-	Yes
9	Colorectal	LH	PR	12	604	150	-	Yes
10	Colorectal	LH	PR (HALS)	10	420	280	-	Yes

IR, ileocecal resection; HAR, high anterior resection; SR, sigmoid resection; LAR, low anterior resection; ISR, intersphincteric resection; LH, left hemicolectomy; PR, partial resection; HALS, hand-assisted laparoscopic surgery.

Table 3 Pathologic data and postoperative outcomes

Case	Pathologic resection margin, +/-	Number of retrieved LNs	Oral fluid intake, POD	Decision to discharge, POD	Morbidity	Time to adjuvant chemotherapy, POD	Recurrence/months of follow-up
1	-	38	2	10	-	32	- / 48
2	-	16	4	16	Ileus, 2*	-	Liver and LNs / 5
3	-	15	2	11	-	67	- / 30
4	-	13	2	13	-	41	Liver / 2
5	-	24	2	16	-	40	LNs / 14
6	-	19	3	11	-	53	- / 32
7	-	10	2	15	SSI, 2*	-	Liver and lung / 6
8	-	19	2	14	-	47	- / 10
9	-	25	3	18	-	53	- / 2
10	-	20	2	10	-	34	- / 54

POD, postoperative day; SSI, surgical site infection; LNs, lymph nodes.

*The Clavien-Dindo grade scale.[15] Grade 1 (requiring oral medications or supportive measures) and Grade 2 (requiring pharmacologic treatment with drugs or bedside treatment, such as replacement of indwelling drainage tube) complications were considered minor. Grade 3 (requiring surgical or radiologic intervention, such as percutaneous computed tomography–guided drainage), Grade 4 (involving long-term disability), and Grade 5 (perioperative death) complications were considered major, based on clinical significance.

CRC with SCRLM, and the optimal treatment strategy remains controversial. However, several recent studies suggest that simultaneous open colorectal and hepatic resection is feasible and can be performed with acceptable morbidity and mortality.[2–4] A recent meta-analysis has confirmed the advantages of a simultaneous open approach, which results in shorter operative time, less blood loss, shorter hospital stays, and reduced morbidity compared with a 2-staged open approach.[21] The surgical option of performing simultaneous laparoscopic colectomy and hepatectomy for primary CRC and SCRLM is now possible thanks to recent improvements in laparoscopic surgery, and this approach has been reported to be feasible in small case series.[5–14]

In staged colectomy and hepatectomy, the results of several studies have supported the use of the "liver first" approach.[22,23] Of note, some have suggested that the growth of the liver metastasis is accelerated by removal of the primary tumor because of changes in tumor homeostasis and removal of angiogenesis-inhibiting factors.[24] Others have suggested that recovery after liver resection is faster and risks reduced by the absence of an anastomosis and potential complications arising from an anastomotic leak.[6] Furthermore, liver metastases are the main determinant of patient prognosis, and hepatectomy thus should be performed first and as soon as possible, particularly if the primary CRC is asymptomatic. However, in a simultaneous colectomy and hepatectomy, no consensus is established; in our series, the decision about which procedure to perform depended first on the surgeon's preference.

The World Consensus Conference on Laparoscopic Surgery has suggested that acceptable indications for laparoscopic liver resection include solitary lesions of 5 cm or less, located in limited liver segments.[25] Moreover, major hepatectomy (more than 3 segments) is reported to independently predict severe morbidity after simultaneous resection of CRC (hazard ratio $= 3.4$, $P = 0.008$).[26] Taking these reports into consideration, in the current study, we limited the indication for simultaneous laparoscopic hepatectomies to those patients with minor liver resection, i.e., tumor size less than 5.0 cm, and up to 3 liver lesions.

An intermittent Pringle maneuver was performed to prevent a major bleeding in 5 patients with multiple hepatic tumors or with tumors that were relatively large and deep in terms of their location. However, special attention should be paid

to prolonged vascular clamping, which causes transient portal hypertension with edema of the intestinal mucosa that ultimately leads to an anastomotic failure. We thus tried to minimize this procedure, and no anastomotic complications developed. On the other hand, we needed to prolong the operative time to confirm adequate hemostasis at the resection surface of the liver.

The key aspects of hepatectomy, which are also the most difficult, are mobilization of the liver and adequate control of blood loss during the transection procedure. The former can be overcome using the HALS technique, which we applied in 2 patients in this study. This technique, in which the surgeon's hand is inserted into the abdominal cavity, is effective not only for retraction and direct manipulation of the viscera but also for exclusion of occult hepatic lesions by palpation.[27] Control of blood loss can be managed using a combination of surgical devices such as a CUSA, a vessel sealing system, and a harmonic scalpel; here, this combination kept blood loss to less than 300 mL in 8 of 10 cases. In fact, a meta-analysis and a multi-institutional study both concluded that laparoscopic liver resection for colorectal liver metastasis is safe, feasible, and efficacious.[28,29] It improves surgical outcomes, and oncologic outcomes are not compromised compared with open liver resection. Moreover, a review of 127 published articles showed that 3-year overall and disease-free survival rates after laparoscopic liver resection for colorectal metastasis to the liver were 80–87% and 51%, respectively.[30] The review concluded that in terms of oncology, long-term outcomes of laparoscopic liver resection for SCRLM are comparable to those of open liver resection. However, randomized controlled trials are still needed to compare laparoscopic and open hepatectomy for SCRLM.

Our data suggest that simultaneous laparoscopic colectomy and hepatectomy for patients with CRC and SCRLM can be performed safely with acceptable morbidity and operative outcomes. Polignano *et al* reported that 13 patients successfully underwent simultaneous laparoscopic resection of primary colorectal tumor and liver metastases with low morbidity and favorable outcomes [median operating time, 370 min (range, 190–540); median blood loss, 50 mL (range, 10–400); rate of postoperative morbidity, 23%].[6] Also, we consider that our result of 13.5 days (range, 10–18) of hospital stay is in an acceptable range compared with previous reports [median hospital stay; Kim *et al* reported 15.5 days (range, 9–27); Huh *et al* reported 10 days (range, 7–30); and Polignano *et al* reported 7 days (range, 3–54)].[5,6,31] Furthermore, we infer that the small incision used for the procedure resulted in less pain and also enhanced recovery, allowing for rapid induction of adjuvant chemotherapy. A laparoscopic approach additionally reduces adhesion formation and facilitates repeat resection in patients who need repeated operation for liver metastases.[7] Finally, an R0 resection along with an adequate number of retrieved lymph nodes showed that good oncologic outcomes were achieved using this approach.

In conclusion, given the limitation that this was a retrospective, noncomparative study with a small patient sample, our data showed that simultaneous laparoscopic colectomy and hepatectomy may be a safe approach and a feasible surgical option for patients with primary CRC and SCRLM. Larger prospective randomized studies are needed to verify these findings.

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