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Simultaneous Laparoscopic Resection of Colorectal Cancer and Synchronous Metastatic Liver Tumor

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Laparoscopic colorectal resection has been applied to advanced colorectal cancer. Synchronous liver metastasis of colorectal cancer would be treated safely and effectively by simultaneous laparoscopic colorectal and hepatic resection. Seven patients with colorectal cancer and synchronous liver metastasis treated by simultaneous laparoscopic resection were analyzed retrospectively. Three patients received a hybrid operation using a small skin incision, 2 patients underwent hand-assisted laparoscopic surgery using a small incision produced for colonic anastomosis, and 2 patients were treated with pure laparoscopic resection. The mean total operation duration was 407 minutes, and mean blood loss was 207 mL. Negative surgical margins were achieved in all cases. Mean postoperative hospital stay was 16.4 days. No recurrence at the surgical margin was observed in the liver. For selected patients with synchronous liver metastasis of colorectal cancer, simultaneous laparoscopic resection is useful for minimizing operative invasiveness while maintaining safety and curability, with satisfying short- and long-term results.

Key words: Colorectal cancer – Colorectal liver metastasis – Simultaneous laparoscopic resection – Laparoscopic colorectal resection – Laparoscopic hepatectomy

Use of laparoscopic surgery for colorectal cancer (CRC) has been increasing rapidly[1,2]; its effectiveness has been established, and its surgical indication has been extended to advanced cases. Liver metastasis occurs in 23% to 29% of CRC patients.[3,4] Thus, CRC with liver metastasis (CRCLM) has become the main condition to be treated laparoscopically.

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Hepatectomy is recommended as the best effective therapy for CRCLM.[5] For synchronous CRCLM, simultaneous resection has been controversial in terms of efficacy and safety because of its surgical invasiveness.[6] However, recent reports suggest the effectiveness of simultaneous resection and establish the safety of hepatectomy.[7–10] Its beneficial effect in shortening total hospital stay has also been reported.[11]

On the other hand, recently acquired surgical skills in laparoscopic hepatic resection have dramatically expanded the surgical criteria for this method of operation. Currently, the proportion of laparoscopic liver resections ranges from 20% to 80% of the total volume of liver surgery performed at a particular center.[12]

In this report, 7 patients with CRC and synchronous CRCLM treated by simultaneous laparoscopic resection and their surgical data were analyzed retrospectively to evaluate the feasibility, safety, and effectiveness of this procedure in terms of short- and long-term results. In addition, reported cases in the literature were reviewed.

Materials and Methods

Patient selection and characteristics

A retrospective study was conducted on 7 consecutive patients undergoing initial simultaneous laparoscopic resection of CRC and synchronous CRCLM with curative intent at Osaka Medical College Hospital from May 2006 to June 2009. Synchronous (as opposed to metachronous) CRCLM was defined as simultaneous presentation of CRCLM before or at the time of the CRC operation. At our institution, laparoscopic colorectal surgery was indicated for patients with CRC, except for those with bulky tumors and cancer invading other organs. In our current protocol, simultaneous laparoscopic resection was indicated for patients without high-risk background diseases, with the hepatic tumor being solitary, less than 5 cm in size, located in the left lateral section or in the right anterior or inferior of the liver (*i.e.*, segments 2–6), and relatively superficial in depth. Patients with excessive lymph node metastasis on preoperative images, including multidetector-row computed tomography, were also excluded. Clinical records and follow-up data of the 7 patients were obtained and retrospectively analyzed. In this study, laparoscopic liver resection was defined as pure laparoscopy, hand-assisted laparoscopy (HALS), and the hybrid technique.[12] Types of hepatectomies were classified according to the Brisbane 2000 terminology.[13]

Operation method

Details of our laparoscopic colorectal resection procedures were described previously.[14] Colorectal resection was done using 5 trocars, and patients were placed in the reverse Trendelenburg position. Trocar placement was determined according to the location of the tumor (*i.e.*, superior mesenteric arterial region versus inferior mesenteric arterial region). The first wound was created at the middle of the umbilicus itself by a vertical 1.5-cm incision. A 12-mm trocar was placed, and the pneumoperitoneum was created. Another 5-mm trocar was placed in the midepigastrium, and two 5-mm trocars were placed in the right upper abdomen, 2 fingerbreadths below the right costal margin in the midclavicular and midaxillary lines, respectively. Colectomy was then performed using a semiflexible laparoscopic camera (LTFVH, Olympus, Tokyo, Japan). Colorectal anastomosis was done by functional end-to-end anastomosis or by the double stapling technique.

After completion of colorectal resection and anastomosis, hepatectomy was performed. Intraoperative ultrasonography (US) was performed routinely beforehand. For the tumor located on the right side of the liver, which required mobilization of the liver, patients were placed in supine or left semidecubitus position. Additional ports were placed when necessary. For left lateral sectionectomy, hepatic round and falciform ligaments were detached, the left triangular ligament was separated, connective tissue was dissected around the inferior vena cava, and thus the left lateral section was mobilized laparoscopically. Hepatic parenchymal resection was performed under an upper middle small skin incision of 7 cm. For the tumor on the right side, the patient was tilted to the left and the lateral side of the right lobe was dissected and mobilized sufficiently; then a subcostal incision of 11 cm was placed followed by partial hepatic resection. We attached the Alexis wound retractor (MEDICAL LEADERS, Tokyo, Japan) to protect and expand the wound. Subsequently, we applied the Kent retractor (Takasago-ika, Tokyo, Japan) to pull the wound in any direction; thus, the surgical field was freely changeable during the operation. Liver parenchymal transection was performed, similarly to the conventional open operation procedure; laparoscopic coagulation shears (LCS) were used for superficial transection, and an ultrasonic dissector (SonoSurg System, Olympus Inc, Tokyo, Japan) was used for deeper parenchymal transection; small vessels (≤3 mm) were coagulated using the tip

attached to the paddle-type electrode of the VIO soft coagulation system (VIO300D, ERBE Elektromedizin, Tübingen, Germany), but bigger vessels (>4 mm) were ligated using a synthetic absorption string or clips. BiClamp was used for hemostasis in the deeper parenchymal transection. For the HALS procedure, the small incision created for colorectal anastomosis extended the wound to 7 cm with Lap Disc (Hakko Medical, Tokyo, Japan) applied to it. A closed-suction type of silicon drain was placed at the anastomotic site.

Chemotherapy

In principle, all patients with CRCLM were given adjuvant chemotherapy. Eligibility criteria in this series included histologically proven adenocarcinoma of the colon or rectum. Patient criteria included an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2. Additionally, patients had to have no serious or uncontrolled concurrent medical illness; no active infection; and adequate hematologic parameters (white blood cell count [WBC] $>4.0 \times 10^3$/L, platelet count $>100 \times 10^9$/L), renal function (serum creatinine $\leq$1.2 mg/dL or calculated creatinine clearance by Cockroft formula $\geq$50 mL/min), and hepatic function (total bilirubin <2.0 mg/dL and aspartate aminotransferase and alanine aminotransferase <100 IU/L). Regimens consisted of 5-fluorouracil (5-FU) alone, 5-FU/leucovorin (LV), 5-FU/cisplatin, tegafur plus uracil (UFT) alone, UFT/LV, oteracil (TS-1), FOLFOX (infusional 5-FU/LV + oxaliplatin), FOLFIRI (infusional 5-FU/LV + irinotecan), and IFL (5-FU/LV + irinotecan).

Patient follow-up

Patients were examined for CRCLM recurrence by US and contrast-enhanced computed tomography (CT) every 4 to 6 months, and blood tests, including tumor markers such as carcinoembryonic antigen (CEA), were given every 2 to 3 months after discharge. When recurrence was suspected, magnetic resonance imaging (MRI) was performed to confirm the appearance of new lesions in the remnant liver, and systemic recurrence was examined by fluorodeoxyglucose-positron emission tomography (FDG-PET) or gallium scintigraphy. Chest and pelvic CT was performed principally every 6 months for local and pulmonary metastasis or recurrence. Recurrence was diagnosed when at least 2 imaging studies confirmed new lesions showing typical features of CRC/CRCLM, when compared with previous images.

Results

A total of 5 men and 2 women were treated. Average patient age at the time of operation was 58.6 years (range, 28–89 years; Table 1). The mean observation period was 18 months (range, 15–43 months). Perioperative mortality was not observed in patients in this study.

Primary CRC was found in the following locations: ascending colon (n = 1), transverse colon (n = 2), sigmoid colon (n = 2), and rectum (n = 3); 1 double cancer patient was identified (Case no.7). CRCLM was located in the following places: segment (S)2 (n = 3), S3 (n = 1), S5 (n = 2), and S6 (n = 1). Hepatectomy consisted of partial resection (n = 5) and left lateral sectionectomy (n = 2). Hepatectomy methods included laparoscopic-assisted open hepatic resection (hybrid) (n = 3) using a small skin incision, HALS using a small incision produced for colonic anastomosis (n = 2), and pure laparoscopic resection (n = 2).

No case was converted to standard open surgery. Negative surgical margins at hepatectomy were achieved in all cases, with a mean surgical margin of 10.8 mm.

Mean total operative time was 407.1 minutes (range, 270–575 minutes), and intraoperative blood loss was 206.7 mL (range, 40–350 mL). Blood transfusion was not required in any case. Hepatic inflow occlusion by the Pringle maneuver was not applied during hepatectomy. Regarding the postoperative course, except in Case no. 1, in which percutaneous drainage for intra-abdominal abscess was required, all patients had no surgical complications. Anastomotic leakage was not observed. Postoperative hospital stay ranged from 7 to 38 days (longest in Case no.1), and average stay was 16.4 days (Table 1). Adjuvant chemotherapy was started at 45.7 days postoperatively on average, except for Case no. 5 because of advanced patient age.

Postoperative recurrence was observed in 3 cases (2 liver, 1 lung), but none of these was detected at the cut surface of the liver.

When results were compared with the historical control of patients (n = 7) undergoing laparoscopic colorectal resection and simultaneous open minor hepatectomy for synchronous CRCLM at our institute, operative time (407.1 versus 360 minutes, lap-hepatectomy group versus open-hepatectomy group, respectively), intraoperative blood loss

Table 1 Patient characteristics and perioperative data

Case	Age, y/sex	Location of CRC	Colorectal operation	Location of CRCLM	Size of CRCLM, cm	Hepatic operation	Operation time, min	Blood loss, mL	Hospital stay, days	Complication	Time to adjuvant chemotherapy, days	Recurrence
Hybrid												
1	67/M	Transverse	Transverse colectomy	S3	3.5	Lateral segmentectomy	520	300	38	Abscess	62	
2	28/M	Rectum	LAR	S2	1.8	Lateral segmentectomy	515	40	21	–	48	Lung
3	72/F	Sigmoid	Sigmoidectomy	S5	2	Partial resection	305	350	11	–	32	Liver
HALS												
4	68/M	Rectum	LAR	S3	2	Partial resection	295	330	14	–	59	
5	89/M	Ascending	Right hemicolectomy	S5	2	Partial resection	370	80	7	–		Liver
Pure												
6	47/F	Sigmoid	Sigmoidectomy	S2	1	Partial resection	270	100	10	–	29	
7	39/M	Transverse/ Rectum	LAR/transverse colectomy	S6	3.4	Partial resection	575	40	14	–	44	
Total*					2.24		407.1	206.7	16.4		45.7	

LAR, low anterior resection.

*Data are means.

(206.7 versus 247.1 mL), postoperative hospital stay (16.4 versus 31.2 days), and surgical complication rates (14% versus 43%) were comparable. A tendency toward a shorter hospital stay was seen in the total laparoscopic group.

Discussion

Laparoscopic liver resection was first described in 1992, and its usefulness has been documented.[15–23] Moreover, laparoscopic major hepatectomy has been reported since 2004.[21,22,24,25] Compared with conventional liver resection, the skin incision is much smaller and the degree of body wall damage is obviously less. Simillis *et al* reported that intraoperative blood loss was decreased in laparoscopic surgery.[26] In addition, Kaneko reported that postoperative recovery was accelerated in laparoscopic surgery.[27] With respect to safety, according to the largest review series from Nguyen *et al*, overall mortality was 9 of 2804 patients (0.3%), morbidity was 10.5%, and no intraoperative deaths were reported.[28] On the other hand, laparoscopic surgery for CRC has been established already and is widely accepted as effective therapy even in advanced cases, such as those with liver metastasis.

The recent advent of simultaneous laparoscopic resection of CRC and synchronous CRCLM is largely a result of the establishment of these 2 laparoscopic procedures. The feasibility and safety of this procedure have been reported since 2006, and it was introduced into clinical practice on the basis of a small case series. Leung *et al* reported a case of simultaneous laparoscopic resection of rectal cancer and liver metastasis with acceptable operative time and blood loss resulting in early postoperative recovery.[29] Geiger *et al* presented a successful case of a 60-year-old male with sigmoid colon carcinoma and synchronous solitary CRCLM treated by simultaneous resection of the sigmoid colon and left lateral liver segment.[30] Bretagnol *et al* reported their preliminary experience with 3 patients who underwent a 1-step totally laparoscopic resection of both colorectal and hepatic cancers, and stated that this procedure was feasible with low morbidity and a short hospital stay.[31] Kim *et al* demonstrated the feasibility of this technique with considerable safety and effectiveness in what is so far the largest series of 10 cases.[32] Patriti reported successful cases of 7 patients undergoing 1-stage laparoscopic or robot-assisted resection with no postoperative morbidity.[33] Akiyoshi *et al* suggested the safety and feasibility of this procedure in selected patients, demonstrating no

major morbidity in 3 laparoscopy-assisted liver resections concomitantly performed with laparoscopic colorectal resections.[34] Huh *et al* reported 7 patients undergoing laparoscopic colorectal resection and simultaneous R0 resection for CRCLM with postoperative short-term advantages.[35]

Advantages of this approach include a shortened recovery period after radical resection, making it possible to induce adjuvant chemotherapy at an earlier stage. In cases of stage IV CRC with synchronous CRCLM, early induction of adjuvant chemotherapy would be mandatory[36]; in this regard, the current approach would have substantial advantages. Actually, in our series, postoperative hospital stay was less than 2 weeks in 5 of 7 cases, and we could start adjuvant chemotherapy on median postoperative day 46, which was a shorter wait than that reported for open hepatectomy simultaneously performed with laparoscopic colorectal resection at our institute (data not shown).

Other plausible advantages of this approach include savings in medical expenditures regarding laparoscopic devices, in that the same devices can be used for both colorectal and hepatic resection. Total cost reduction would not be ignorable because the second hospitalization for hepatectomy becomes unnecessary by virtue of this applied procedure. In addition, an earlier return to usual function as a result of more rapid recovery would benefit patients economically. One of the ancillary advantages is reduced adhesion associated with this approach, especially in cases in which subsequent re-hepatectomy is anticipated.[37] Using the small wound created for colorectal anastomosis as the route for removal of a liver specimen would facilitate the procedure.

However, many obstacles still remain with respect to technical aspects. Although previous reports have suggested that laparoscopic hepatectomy offers the advantage of decreased intraoperative blood loss, adequate control of blood loss especially during hepatic parenchymal transection still represents the key point of this procedure. In our series, by using multidevices during the transection procedure, blood loss during the whole colorectal and hepatic resection could be decreased to less than 100 mL in 4 of 7 cases. In terms of secure hemostasis, the HALS technique would provide the advantage of facilitating this process more safely.[38,39]

In this series, the Pringle maneuver was not applied during hepatectomy. The potential risk of this maneuver is a topic of controversy,[40] although enhancing the risk of anastomotic leakage caused by intestinal edema is theoretically plausible. Actually, in cases of low anterior rectal resection, the mortality rate has been high as the result of anastomotic leakage.[41] In our series, because bleeding during hepatic transection was relatively well controlled, inflow occlusion was not required; thus median intraoperative blood loss was 206 mL and no anastomotic leakage occurred. In this context, more complicated cases, such as larger tumors, multiple tumors, or deeply located tumors—which we did not include as indications in this series—would be forthcoming challenges.

Lack of bimanual palpation examination to exclude occult hepatic metastatic lesions is one of the unavoidable issues associated with this procedure. HALS may resolve this problem in part, but its usefulness is limited in most cases. Practically, thorough and vigorous examination using intraoperative laparoscopic US would be the only way to address the apparent disadvantage of this procedure so far.[42] Moreover, US observation prior to hepatectomy would avoid unnecessary operation thereafter, because a 10% to 25% detective rate has been reported with the use of intraoperative US in cases in which preoperative CT failed to detect the presence of occult CRCLM.[43–47]

The other notable disadvantage of this procedure compared with open surgery is the theoretical difficulty of obtaining a negative hepatic margin, although the problem is not unique to this simultaneous procedure. In particular, with the use of pure laparoscopic technique, deliberate confirmation of surgical margins of the liver would be required with vigorous use of intraoperative US.

Although satisfying short-term results have been reported, information regarding long-term outcomes is scarce to date. In our study, although the observation period was limited, the recurrence rate was comparable with those in cases of open hepatectomy (data not shown). In addition, local recurrence at the cut surface of the liver was not observed. Because randomized study on open versus laparoscopic surgery was not performed, and because the sample size in this study was small, statistical analysis was not available; however, when an appropriate indication is held, this approach would not present substantial risk of enhancing the recurrence rate. Further study, including a randomized controlled study, will be needed to clarify this matter.

The optimal indication for this procedure needs to be established. In the current study, we limited the indication for simultaneous hepatectomy to those patients with CRCLM of a solitary tumor, smaller than 5 cm, and relatively peripheral and superficial in location (*i.e.*, segments 2–6), because

these are considered universally acceptable criteria for safe laparoscopic hepatectomy to date.[12] Further expansion of these criteria to more challenging CRCLM cases is anticipated in accordance with accumulation of experience with laparoscopic hepatectomy; nonetheless, care should be taken to avoid compromising the simultaneously resected and anastomosed colon or rectum, as well as the patient *per se*. In this context, laparoscopic major hepatectomy, defined as resection of 3 or more Couinaud segments (which would often necessitate the Pringle maneuver), and hepatectomy for liver in the parenchyma (which is occasionally compromised because of the effects of neoadjuvant chemotherapy)[48] need to be adequately and deliberately addressed as indications for this procedure.

Although simultaneous resection of CRC and initially resectable CRCLM has been advocated because of the benefits of avoiding a second operation and reducing morbidity, whether simultaneous resection for synchronous metastasis is superior to a staged operation after a certain interval as a ''waiting time'' remains a topic of controversy.[7,49–53] Given that liver metastatic lesion(s) would occasionally emerge or would be detected on follow-up despite their not appearing at the first presentation of metastasis, a laparoscopic approach would offer advantages to some extent by reducing operative stress and postoperative adhesion, should re-hepatectomy become necessary. With regard to multiple metastases, which were excluded from the indication in our current protocol, further study is necessary to determine the appropriateness of including this status as an indication for the procedure, taking into consideration that both recurrence rate and technical difficulty would be aggravated by these conditions.[8,54]

In conclusion, for selected patients with CRC and synchronous CRCLM, simultaneous laparoscopic resection would provide good outcomes in terms of early postoperative recovery without enhancing surgical risk, as well as acceptable long-term outcomes, including reducing recurrent disease.

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