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ORIGINAL ARTICLE

Long term outcomes of simultaneous laparoscopic versus open resection for colorectal cancer with synchronous liver metastases

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Summary *Background/Objective:* Because of the advancements in the surgical techniques of liver resection and improvements in anesthesia and postoperative critical care, the simultaneous resection of synchronous colorectal cancer with liver metastasis either by the laparoscopic procedure or by the open resection method has been considered as a safe and acceptable option. However, there is limited information on the comparison of postoperative outcomes between laparoscopic surgery and open surgery. This study investigated the clinical results and postoperative outcomes of laparoscopic simultaneous resection of synchronous colorectal cancer with liver metastasis in comparison with those of open surgery.
Methods: Patients with synchronous colorectal cancer and liver metastasis who underwent simultaneous resection at Shuang Ho Hospital from 2009 to 2017 were identified. The patient demographics, perioperative morbidity, and survival rates were analyzed.
Results: A total of 38 patients underwent simultaneous resection of synchronous colorectal cancer with liver metastasis. Laparoscopic procedure was performed for 16 patients, and the remaining 22 patients underwent open surgery. No significant differences were observed in the patient characteristics between the two groups. There was no perioperative mortality

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in both groups. The 1- and 3-year disease-free survival rates were 56% and 35% in the laparoscopic group and 70% and 15% in the open surgery group, respectively. The 1- and 3-year overall survival rates were 100% and 84% in the laparoscopic group and 73% and 48% in the open surgery group, respectively.

Conclusion: In selected patients, laparoscopic surgery for simultaneous resection of synchronous colorectal cancer with liver metastasis seems to be safe and had a similar outcome to that of open surgery.

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1. Introduction

Colorectal cancer (CRC) is one of the most common cancers in Taiwan and is also the third most cause of death in patients with cancer.[1] The liver is the most common site for CRC metastases. Approximately 15%–20% of patients with newly diagnosed CRC will be found to have synchronous liver metastasis (LM).[2] The optimal treatment strategy for resectable CRC and LM is complete surgical removal of primary tumor and all liver metastatic tumors. Complete surgical resection all tumors remains only potential curative treatment option.[3,4] Staged surgery was first developed and performed; resecting liver lesions 6 weeks to 6 months after resection of the primary colorectal tumor had lower morbidity and mortality rate compared to synchronous resection of CRC and LM.[5–7] However, with improvements in the surgical skills and surgical apparatus, simultaneous resection of CRC and LM is being widely used today. Simultaneous resection of CRC and synchronous LM has been proved to be safe with similar long-term cancer outcomes compared to those of staged procedures.[8] Other advantages of simultaneous resection include fewer days of hospitalization and being cost-effective.[9]

In recent two decades, minimally invasive surgery such as laparoscopic or robotic surgery had been widely applied in colorectal and hepatobiliary surgery. Laparoscopic colectomy now considered as the standard treatment for benign or malignant colorectal disease. Laparoscopic hepatectomy for CRC with LM also had some short-term benefits such as less blood loss and fast recovery and also had comparable oncologic outcomes as in open liver resection.[10–17]

Although laparoscopic surgery had many benefits either in colorectal or hepatobiliary surgery, laparoscopic combination resection for primary colon cancer and liver metastasis is not commonly conducted. In a recent European multicentre study including 450 elderly patients with colorectal liver metastases after propensity score matching, the rates of synchronous resections were 5% for laparoscopic group and 6% for open group.[18] Only a few comparisons of the outcomes between laparoscopic surgery and open surgery methods in patients undergoing synchronous surgery.[19–21] Therefore, this study was performed to assess the short- and long-term outcomes of these patients.

2. Materials and methods

2.1. Study population

We reviewed the medical charts of patients with a preoperative diagnosis of CRC and suspected LM who underwent synchronous resection of CRC and liver tumor from Jan 2009 to Dec 2017. Totally, 38 patients were identified, 16 patients underwent laparoscopic surgery and 22 patients underwent open surgery. We analyzed patients characteristics and peri-operative short-term outcome in these 38 patients. In oncological Long-term outcome, we excluded patients with liver tumor not metastatic CRC and also excluded patients with metastatic tumors being also found in other organ not only in the liver. Finally, 30 patients were identified, 15 patients underwent laparoscopic surgery and other 15 patients underwent open surgery (Fig. 1).

2.2. Surgical technique

Colorectal resection was performed first, followed by liver resection. Briefly, in the laparoscopic group, the medial-to-lateral approach with extracorporeal resection and hand-sewn anastomosis was performed in the right-sided colon resection. For the left-sided colon resections, the medial-to-lateral approach with stapled-instrument resection and stapled anastomosis was performed. The resections were performed following the principles of high ligation of feeding vessels and total mesorectal excision for rectal cancer resections.

In the liver resection, intraoperative ultrasonography was applied for all patients to assess the metastatic lesion. Cavitron ultrasonic surgical aspirator and bipolar scalpel were used to perform liver dissection. The Pringle maneuver was used in right lobectomy or segmentectomys which contains segment 7 or 8. The main vessels such as portal vessels or hepatic vein where ligated by hemolock or stapled instruments. The specimen were retrievaled from umbilicus trocar wound or left lower abdominal tracer wound. The localization of trocars and number of ports were show in Fig. 2.

All postoperative complications were reviewed for at least 30 days following the surgery. The complication were classified from grade 1 to grade 5 according to Clavien-Dindo classification of surgical complication.

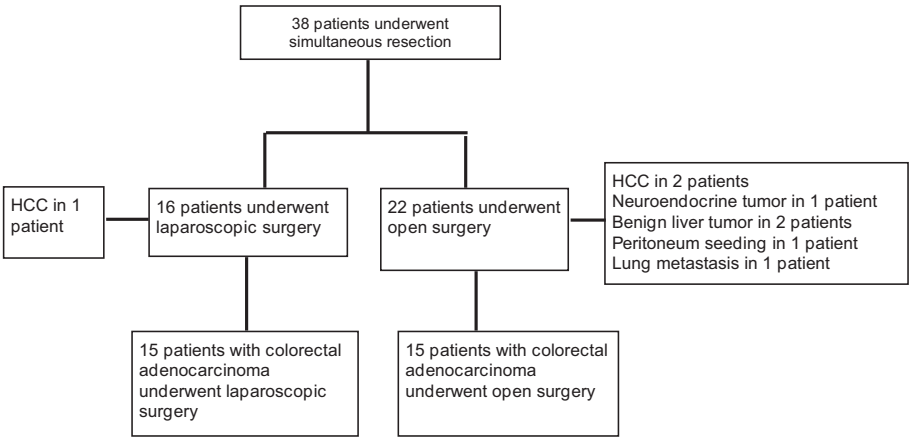

Figure 1 Patient selection flow diagram.

2.3. Statistical analysis

Data were analyzed using the Statistical Product and Service Solutions 20.0 package for Macintosh (SPSS Inc., Chicago, IL, USA). Results were presented as mean ± standard deviation. The overall survival and disease-free survival were determined using the Kaplan—Meier method. Comparisons were made using the χ^2 test or one-way ANOVA for categorical or continuous variables, respectively, and a p value < 0.05 was considered to be statistically significant.

3. Results

A total of 38 patients were identified. Of the 38 patients 16 patients underwent laparoscopic surgery and the remaining 22 patients underwent open surgery. One patient was scheduled for laparoscopic surgery but was converted to open hepatectomy due to tumor location and size (S2, S6, and S7 and 5, 7, and 5 cm).

The characteristics of these patients are shown in Table 1. No statistically significant differences were observed between both groups in age, gender, American Society of Anesthesiology (ASA) score, body mass index (BMI), primary tumor characteristics, and liver tumor characteristics (Table 1). However, the carcinoembryonic antigen level in the laparoscopic group was higher than that in the open surgery group (929 ± 1936 vs 247 ± 728, $p = 0.01$). In liver tumor pathology, six patients were not metastatic adenocarcinoma, three were hepatocellular carcinoma, one is neuroendocrine tumor and the other two is benign liver tumor.

Regarding the perioperative outcomes, there were no significant differences between both groups in the operation method, blood loss, postoperative complications, length of hospital stay. The operative time in laparoscopic surgery was longer than open surgery (320 ± 124 min VS 227 ± 55 min $p = 0.04$). (Table 2).

In oncological long-term analysis, we excluded six patients with liver tumor not metastatic CRC and also excluded two patients with metastatic tumors being also found in other organ not only in the liver(Fig. 1). Finally, 30 patients were analyzed, 15 patients underwent laparoscopic surgery and other 15 patients underwent open surgery. The median follow time in laparoscopic group was 19months (1—70 months) months and 13months (1—95 months) in open group. Table 3 shows the postoperative outcomes and survival rates between the two groups. No differences in the disease-free survival rates and overall

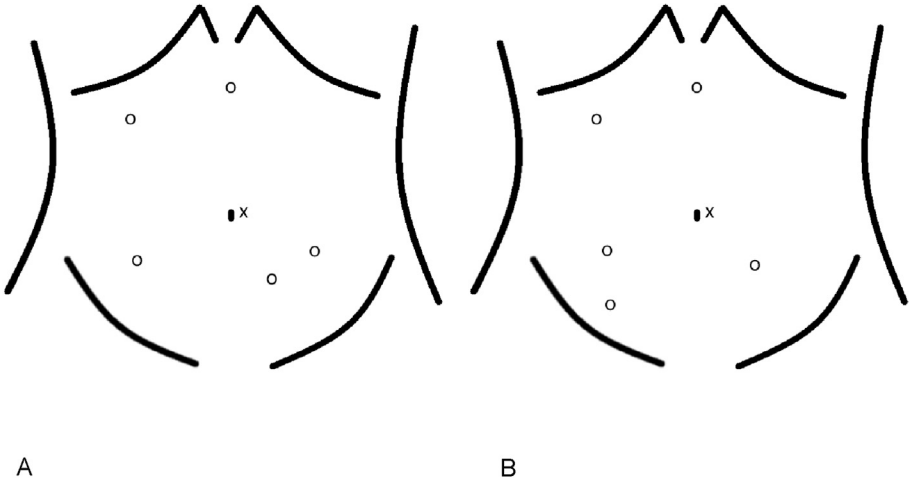

Figure 2 Trocar site. A. Right side colectomy B. left side colectomy X. camera port O. assistant port.

Table 1 Patient characteristics.

	Laparoscopic (n = 16)	Open (n = 22)	*p* - value
Age (year)	66.0 ± 10.4	64.8 ± 13.0	0.46
Gender Male/female	10/6	9/13	0.20
ASA score, mean (range)	1.9 (1–3)	2.0 (1–3)	0.49
CEA	929 ± 1936	247 ± 728	**0.01**
BMI	23.8 ± 3.7	23.3 ± 4.1	0.44
Primary tumor Size (cm)	4.0 ± 2.0	5.0 ± 3.0	0.05
Venous invasion	10	15	0.72
Perineural invasion	4	11	0.13
Primary tumor			
TNM stage			0.84
T1	1	1	
T2	1	1	
T3	11	16	
T4	4	4	
N0	4	7	
N1-2	12	15	
Lymph node harvesting	24.5 ± 9.2	32.0 ± 19.5	0.42
Liver tumor			
Number of tumor			0.23
1	8	17	
2	4	2	
>=3	4	3	
Liver tumor pathology			
Metastatic adenocarcinoma	15	17	
Hepatocellular carcinoma	1	2	
Neuroendocrine tumor	0	1	
Benign tumor	0	2	
Largest tumor size (cm)	5.5 ± 4.2	4.7 ± 3.7	0.99
Tumor location only at S2,3,6	4	7	0.37

survival rates were observed between the two groups. The disease-free survival and the overall survival curves are shown in Figs. 3 and 4, respectively.

4. Discussion

Traditionally, staged resection of CRC and LM has been the standard approach in resectable patients.[22] This typically comprises resection of the primary tumor, followed by chemotherapy, and, if there is no progression of the metastatic disease, a subsequent planned liver resection will be performed. Furthermore, several studies have reported that the long-term outcomes in terms of overall survival and disease-free survival are similar between the simultaneous and delayed resection groups.[23–25] The advantages of simultaneous resection include fewer days of hospitalization, decreased medical expenses, and the need for only one surgery to remove the tumors.[23] Therefore, the paradigm for the surgical management of synchronous LM of colorectal cancer appears to be moving toward simultaneous resection.

Laparoscopic surgery had better cosmetics and faster recovery than conventional open surgery either in colectomy or hepatectomy. The long-term outcome of colon cancer after minimally invasive surgery is equivalent to that after open surgery, the same results were also noted in liver cancer treated by minimal invasive hepatic resection.[26–28] But for the synchronous laparoscopic resection of CRC and LM, few studies have focused on it. In our study, the average operative time was shorter in the open surgery group than in laparoscopic surgery group, and there was no difference between the blood losses. Takasu et al[29] reported a similar result in the operative time but more blood loss in the open surgery group. Lin et al[30] reported a longer operative time in the laparoscopic group, but the estimated blood loss was lower in this group. The possible reasons included the surgical technique and the apparatus. In addition, the operations in our study were mostly performed by one colorectal surgeon and one hepatobiliary surgeons, which decreased the bias between different surgeons.

The advantages of synchronous laparoscopic resection of CRC and LM are known to be the decreased damage and the reduced wound length in abdomen. In conventional open surgery, it usually needs a long midline wound from xiphoid process to the pubic symphysis for an adequate abdominal approach, especially the combination of sigmoid colon or rectal resection and simultaneous liver resection. The shorter length of incision may lead to less postoperative pain, faster gastrointestinal recovery, and reduced bowel adhesion. In our study, there was no significant difference in hospital stay between the two groups, this is mainly because we all wait until patients had well tolerant oral

Table 2 Peri-operative characteristics of the patients in two groups.

	Laparoscopic (n = 16)	Open (n = 22)	*p* - value
Colorectal Operation method			0.74
Right hemicolectomy	4	8	
Left hemicolectomy	0	1	
AR	6	3	
LAR	6	9	
Subtotal colectomy	0	1	
Liver operation method			0.78
Wedge	5	7	
One segmental	6	9	
Two segment	2	3	
(>=3 segment)	3	3	
OP time (minutes)	320 ± 124	227 ± 55	**0.04**
Blood loss (ml)	369 ± 400	325 ± 260	0.27
Number of Pringle maneuver	5	7	
Conversion (%)	1 (6.3)		
Post-operative complication			0.06
Wound infection	1	2	
Paralytic ileus	1	3	
Pleuropulmonary	1	1	
Intraabdominal abscess	1	2	
Clavien-Dindo classification			
Grade 1	1	2	
Grade 2	2	3	
Grade 3	1	3	
Hospital days	11.6 ± 5.2	12.7 ± 6.4	0.67

diet before he is discharged. Eight of 22 (36%) patients in open surgery had post-operative complication, though there was no significant higher than laparoscopic surgery. This is because our patients number is small.

In the present study, the 1- and 3-year overall survival rates were 100% and 70% in the laparoscopic group and 90% and 51.4% in the open surgery group, respectively. Lin et al have also reported similar survival rates.[19] Other previous studies have reported that approximately 25%—50% of patients would survive for more than 5 years.[30—32]

Bleeding is one of a difficulty in liver resection and Pringle maneuver is needed to make decrease blood loss by transient liver blood inflow control. Liver pedical clamping also causes portal hypertension and it can lead to an increased risk of anastomotic leakage because of the onset of intestinal edema.[33] Intra-operative hypotension was

Table 3 Outcome and survival.

	Laparoscopic (n = 15)	Open (n = 15)	*p* - value
Median follow (months)	19	13	0.91
Disease free			0.99
Mean (month)	13	10	
1 year	0.56	0.70	
3 year	0.35	0.15	
Overall survival			0.14
Mean (month)	26	22	
1 year	1.00	0.84	
3 year	0.73	0.48	
Adjuvant chemotherapy	12	13	
Recurrence	8	8	1.00
Death	2	5	0.09
Site of initial recurrence			0.85
Liver	6	6	
Lung	1	1	
Peritonium	0	1	
Adrenal gland	1	0	

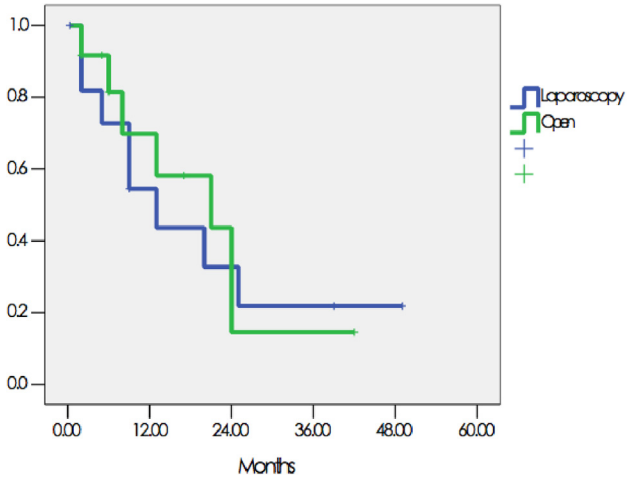

Figure 3 Disease Free survival curve in two groups ($p = 0.85$).

usually occurred in hepatectomy because of more blood loss when performing liver resection, and it also increased the risk of anastomotic leakage.[34] Our patients underwent hepatectomy after colon resection. So 12 patients underwent Pringle maneuver either in laparoscopic group or open group after colon resection, and there was no anastomotic leakage in our study. This possible reason is every time we clump the liver pedical only five to 10 min then resume the blood flow for 5 min, and it caused less edema in anastomotic site. So we suggests that colon resection first in simultaneous resection of CRC and LM can be performed without increased anastomotic leakage.

In our clinical practice, 6 of 38 patients with concurrent colorectal resection and hepatectomy were found to have tumors of the liver that were not metastasized from CRC. Three patients were diagnosed with both CRC and hepatocellular carcinoma based on the pathological report. Sun et al reported that CRC was accompanied by a second primary cancer in 5.3% of the patients.[35] Because patients do not receive simultaneous resection of CRC and LM in staged operation, and then chemotherapy for CRC is not effective for other malignant tumors in the liver, especially hepatocellular carcinoma. An accurate diagnosis of the liver tumor

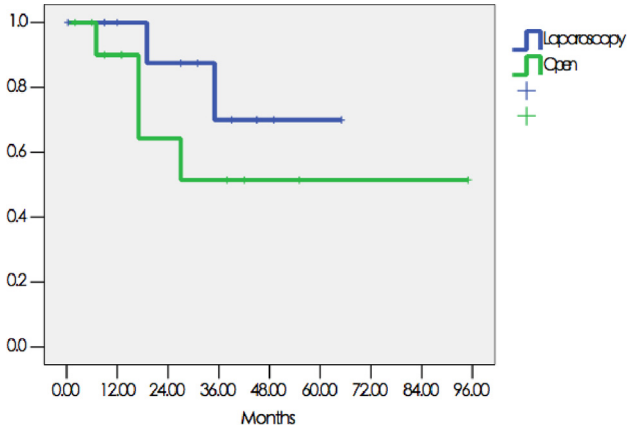

Figure 4 Overall survival curve in two groups ($p = 0.26$).

in patients with CRC is important; however, a liver biopsy before the operation is not recommended because of the potential spread of the peritoneum due to tumor rupture and other imaging studies such as computed tomography and magnetic resonance imaging have reported a false-positive rate of 3%—8%.[36,37] This is why we believe that it is better to perform the simultaneous resection of CRC and liver tumor, if possible, to minimize the risk of multiple surgeries and reduce a misdiagnosis.

Although simultaneous resection of CRC and LM had some benefits, and not all patients are suitable for synchronous resections. The timing and sequence of operations in patients with synchronous CRC and LM do need to be tailored based on patient-, surgeon- and hospital-specific factors. Generally speaking, patients with a rectal tumor, or patients with a large burden of liver disease requiring two-stage hepatectomy, and perhaps some patients with marginal performance status, may be better served by a staged approach, and other patients with better general performance, can seemingly be managed with a simultaneous surgery approach.[9] So a good preoperative risk evaluation can make us better to determine the treatment plan of these patients. Madhavan, et al recently reported that using the ACS-NSQIP risk score to predict the risk of hepatic resection had a more accurate predictive rate.[38] So we suggest that we can use this predictive system to determine patient acceptance of staged operations or simultaneous operations.

In conclusion, both laparoscopic and open surgeries are safe and effective for simultaneous resection. There were no differences in the postoperative outcomes and survival rates between the two groups. It is necessary to conduct further studies using a large number of case series or a randomized controlled trial for evaluating the postoperative outcomes and the long-term oncological results.

Conflict of interest

Dr. Ying-Wei Chen, Ming-Te Huang and Tung-Cheng Chang have no conflicts of interest or financial ties to disclose.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.asjsur.2018.04.006.

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