

Original Article

The Short-term Outcomes of Laparoscopic Radiofrequency Ablation Combined with Hepatic Resection versus Hepatic Resection alone for Patients with Colorectal Liver Metastases

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Key Words

Colorectal cancer;
Liver metastasis;
Hepatectomy;
Radiofrequency ablation

Purpose. Though hepatic resection (HR) is the standard local therapy for patients with colorectal cancer liver metastases (CRLM), radiofrequency ablation (RFA) may be an alternative therapy for older adult patients, small (< 3 cm) solitary lesions, unresectable lesions and vulnerable patients with medical comorbidities or poor surgical risk. This study aimed to compare the short-term prognosis of laparoscopic HR combined with RFA versus laparoscopic HR alone for treatment of CRLM.

Materials and Methods. This retrospective study enrolled 40 patients with CRLM who underwent laparoscopic HR at Chi Mei Hospital between 2019 and 2022. Twenty patients underwent laparoscopic HR combined with RFA, and 20 patients underwent laparoscopic HR alone. Patients' demographic and clinical data, including perioperative/operative details, tumor-related parameters, and postoperative outcomes, were analyzed retrospectively.

Results. In the HR-plus-RFA group, the operation times and postoperative hospital stays were significantly shorter than those in the HR-alone group. However, no statistically significant between-group differences were found in blood loss and number of blood transfusions. No statistically significant differences were noted in 1-year overall survival and cancer-specific survival between the two groups ($p = 0.127$; $p = 0.346$). However, 1-year disease-free survival was significantly lower in the HR-plus-RFA group (35%) than in the HR-alone group (80%) ($p < 0.001$). In univariate and multivariate analysis, CRLM treatment methods were independent prognostic factors for tumor recurrence ($p = 0.019$).

Conclusions. When compared to hepatic resection alone for liver metastases in colorectal cancer, surgical resection combined with radiofrequency ablation (RFA) significantly reduces the operation time and in-hospital stay with a comparable short-term (one-year) survival but the tumor recurrence rate is higher than that in patients receiving hepatic resection alone.

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Colorectal cancer (CRC) is the third most frequently diagnosed cancer and has the second highest mortality rate worldwide, accounting for one-tenth of all cancer cases and cancer-related deaths annually.¹ Similarly, colorectal cancer is the most common cancer in Taiwan,² and the liver is the most vulnerable metastatic site due to its special blood supply and anatomic location.³ Approximately 25% of CRC patients have colorectal cancer liver metastases (CRLM) at initial diagnosis, 50% of these patients will develop liver metastases (CRLM) in their lifetime, and liver metastases contribute to mortality in two-thirds of CRC cases.⁴⁻⁶ Despite hepatic resection (HR) being the “gold standard” of treatment for CRLM, the majority of patients are not candidates for resection due to unresectable disease, presence of extrahepatic disease, or patients’ comorbidities.^{5,7} Only fewer than 20% of patients are candidates for surgical resection, while surgery is not appropriate for most patients due to extensive liver disease or concurrent medical condition. Accordingly, these patients often can only undergo chemotherapy, with poor long-term prognosis.⁸

Furthermore, therapeutic modalities for liver metastases can be divided into surgical resection, non-resection ablation techniques, and regional or systemic chemotherapy. Management of CRLM has changed significantly during the past decade. Improvements in operative management, better knowledge of liver hypertrophy, and advances in surgical skills have led to increased safety in liver resection.⁹ Acquiring new knowledge to improve surgical results have focused on minimizing blood loss and maintaining appropriate functional remnant liver volume. Over recent decades, many efforts have been made to increase the number of patients with potentially resectable CRLM. The advent of more effective chemotherapy, specific techniques such as portal vein embolization and local ablation therapy, including radiofrequency ablation (RFA), and also two-staged hepatectomy have expanded the indications for surgery in patients with CRLM and have offered a substantial survival benefit to selected patients.¹⁰

However, numerous studies have reported that RFA was inferior to hepatectomy in the treatment of CRLM, in terms of both local control and survival.¹¹⁻¹³

In essence, little evidence is available to support the routine use of RFA in the management of CRLM, even in combination with hepatectomy. The aim of current study was to compare clinical outcomes between laparoscopic HR combined with RFA and laparoscopic HR alone in treating CRLM.

Materials and Methods

Study design

This retrospective study enrolled 40 patients with CRLM who underwent laparoscopic HR at Chi Mei Hospital between January 2019 and July 2022. Among 1665 patients diagnosed with CRC, 198 patients were diagnosed as clinical stage IV. Of these, 83 patients were diagnosed as CRLM, and details of these cases were reviewed retrospectively, as shown below.

Patient selection and definitions

For the purpose of this study, the primary tumor location was divided into three groups: right-side colon, left-side colon, and rectum. The right-side colon includes the cecum, ascending colon, hepatic flexure, and proximal two thirds of the transverse colon; and the left colon includes the splenic flexure, distal third of the transverse colon, descending colon and sigmoid colon. The diagnosis of liver metastasis was based on the results of imaging studies such as ultrasonography and enhanced computed tomography, or magnetic resonance imaging with/without needle biopsy. Needle aspiration biopsy was performed before treatment only in patients with atypical hepatic mass enhancement. Liver metastases were defined as synchronous whenever they were diagnosed before colorectal resection.

Resectability was defined by experienced hepatobiliary surgeons and a radiologist as the ability to immediately achieve complete resection (R0) with an adequate future remnant liver. The estimated liver volume following hepatic resection was established as > 30% of the total estimated liver volume. The safety limit for the liver parenchymal resection rate was estimated using ICG-R15 and Makuuchi criteria to select

patients for hepatectomy. Hepatobiliary surgeons determined the appropriate surgical procedure.

Since 2005, a weekly colorectal multidisciplinary team meeting has been held at Chi-Mei Hospital, during which cases of all newly diagnosed patients are discussed. During January 2019 to July 2022, 57 patients underwent simultaneous surgical procedures for colorectal cancer and liver metastasis. Perioperative staging, operative records, and final pathology reports were reviewed for all 57 patients. Exclusion

criteria included: 1. Patients who underwent non-curative surgery (liver R2 resection); 2. Patients who received open or Da Vinci-assisted surgery; 3. Patients who received laparoscopic microwave treatment for multiple liver metastasis instead of RFA. Finally, after exclusions, 40 patients were enrolled in this study (Fig. 1), among whom 20 cases received laparoscopic HR only (HR-alone group) and 20 cases received simultaneous laparoscopic RFA and HR (HR-plus-RFA group).

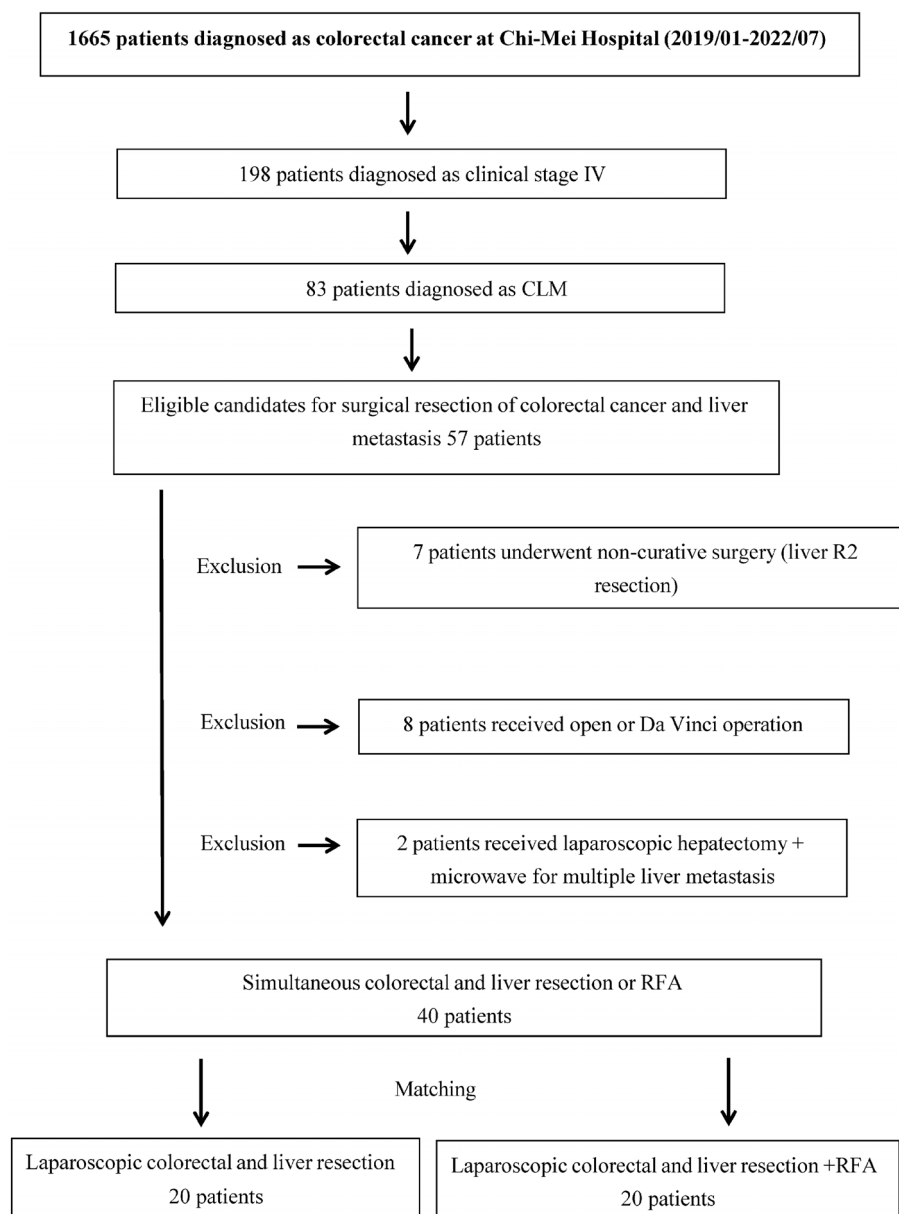


Fig. 1. Diagram of study flow.

Preoperative management

Briefly, before hepatectomy, all patients underwent routine laboratory tests, including measurement of serum carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9 levels, and liver function tests. Thoracoabdominal and pelvic imaging (ultrasonography, CT and/or MRI) were performed to determine disease stage. Preoperative chemotherapy was administered to patients with initially unresectable CRLM in a conversion setting, or to patients with synchronous (diagnosed before, during or within 3 months after colorectal resection) or marginally resectable CRLM in a neoadjuvant setting. The response to preoperative chemotherapy was evaluated after every four cycles of treatment by CT, according to the Response Evaluation Criteria in Solid Tumours (RECIST).¹⁴ Criteria for unresectability were based mainly on the inability to perform curative surgery with a single hepatectomy leaving at least 30 percent of non-tumoral liver parenchyma, or 40 percent after prolonged chemotherapy (more than 8 courses). The final decision to undertake surgery was made during a multidisciplinary team meeting, including surgeons, medical oncologists and radiologists.

Surgical strategy

The objective of surgery was to remove all detectable lesions with a tumor-free margin. If a tumor-free margin was not possible because of contact with major vascular or biliary structures, resection was still considered provided that all tumors could be resected macroscopically.¹⁵ If removal of all tumors cannot be achieved by single hepatectomy, specific techniques, such as RFA, were added. RFA was, in principle, performed in patients with a maximum tumor diameter in the remnant liver of less than 30 mm. RFA was performed using the COVIDIEN Cool-tip™ RF Ablation System E-Series (Medtronic, Minneapolis, MN, USA). The electrode was inserted under ultrasonographic guidance for deeply located tumors or under direct visual guidance for subcapsular lesions. After insertion of the electrode, ablation was started with a gradual increase in power from 60 W to 100 W. The duration

of ablation was determined by achievement of the roll-off effect (decreased power and increased impedance) depending on the target lesion's characteristics. According to empirical guidelines, the ablation diameter is around 2 cm, requiring approximately 8 minutes, while an ablation diameter of 3 cm typically requires around 12 minutes. The hyperechoic area of the treated tumors was monitored with ultrasonography. During hepatectomy, RFA was used for the treatment of inaccessible or deeply located tumors to spare the maximal liver parenchyma.

Postoperative evaluation

All postoperative complications were graded according to the Dindo-Clavien classification.¹⁶ A major complication was defined as any complication of grade III or higher. After treatment, all patients underwent regular follow-up to monitor serum CEA and CA19-9 levels, and imaging studies, including ultrasonography and abdominal and thoracic CT (alternately) to detect any intrahepatic or distant recurrence. Spiral CT in the arterial and portal phases, and measurement of the density of treated lesions before and after arterial injection, was performed at 1 month and then every 3 months thereafter. Local recurrence after hepatectomy was defined as tumor recurrence at the resection margin.

Statistical analysis

Categorical variables were compared using either Pearson's chi-squared test or Fisher's exact test. Continuous variables were analyzed using the student's t-test. Logistic regression analysis was used to determine the independent predictors of overall survival and progression-free survival using the significant parameters in univariate and multivariate analyses. Survival analyses were done using the Kaplan-Meier method, with comparisons by means of the log rank test. Overall survival (OS) was calculated from the date of hepatectomy until death or last follow-up. Progression-free survival (PFS) was defined as the time between curative surgery (hepatectomy or resection of concomitant extrahepatic disease if present) and first

recurrence or death. *p*-values less than 0.05 were considered statistically significant. All statistical calculations were carried out using IBM SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA).

Results

Patients' demographic and clinical data

A total of 40 patients receiving laparoscopic liver resection for CRLM were enrolled in this study. Twenty patients received laparoscopic hepatic resection combined with radiofrequency ablation (HR-plus-RFA group) and the other 20 patients received laparoscopic hepatic resection alone (HR-alone group). The demographic and clinicopathological characteristics for all

40 patients are listed in Table 1. The HR-plus-RFA group had the predominant number and status including multifocality and bilobar involvement of liver metastasis (*p* < 0.001). No significant differences were found between the two groups in the other observed parameters, including mean age, sex, pre-OP CEA level, primary tumor location, the tumor size of CRLM, pathology T/N status, percentage of adjuvant chemotherapy (Table 1).

Perioperative outcomes

Overall operative features focused on the perioperative procedure and post-operative complications, as shown in Table 2. The operation times in the HR-plus-RFA group were significantly shorter than those in the HR-alone group [(289.40 ± 148.154) min vs.

Table 1. Characteristics of 40 CRLM patients in the HR-alone and HR-plus-RFA groups

	HR (N = 20), N (%)	HR + RFA (N = 20), N (%)	<i>p</i> -value*
Age			0.552
Means ± SD	60.55 ± 13.25	58.35 ± 9.626	
Sex			0.168
Male	12 (60.0%)	16 (80%)	
Female	8 (40.0%)	4 (20%)	
Pre-op CEA (ng/ml)			0.464
Means ± SD	45.94 ± 137.38	84.18 ± 185.83	
Primary tumor location			0.917
Right side	3 (15.0%)	3 (15.0%)	
Left side	14 (70.0%)	13 (65.0%)	
Rectum	3 (15.0%)	4 (20.0%)	
Number of liver metastases			< 0.001
≤ 3	17 (85.0%)	4 (20.0%)	
> 3	3 (15.0%)	16 (80.0%)	
Largest liver metastasis (cm)			0.736
≤ 3	13 (65.0%)	14 (70.0%)	
> 3	7 (35.0%)	6 (30.0%)	
CRLM status			< 0.001
Multifocality	10 (50.0%)	20 (100.0%)	
CRLM status			< 0.001
Bilobar involvement	8 (40.0%)	18 (90.0%)	
Pathology T stage			0.077
1-3	19 (95.0%)	15 (75%)	
4	1 (5.0%)	5 (25%)	
Pathology N stage			1.00
0	5 (25.0%)	4 (20%)	
1-2	15 (75.0%)	16 (80%)	
Neoadjuvant chemotherapy	4 (20.0%)	15 (75.0%)	< 0.001
Adjuvant chemotherapy	20 (100.0%)	20 (100.0%)	1.00

(194.00 ± 66.243) min; $p = 0.012$]. For blood loss, no significant differences were found in either group [HR-plus-RFA group (460.00 ± 506.17) microliters vs. the HR-alone group (657.50 ± 545.86) microliters; $p = 0.243$]. A similar trend toward intra-operative blood transfusion was found in both groups (11 transfusions [55.0%] in the HR-plus-RFA group and 13 transfusions [65.0%] in the HR-alone group, $p = 0.623$). Mean operative blood loss and blood transfusion during surgery were not significantly different between the two groups. Besides, there were a total of 13 segmentectomies and 66 wedge resections, with a mean surgical margin of 3.71 mm in the HR-plus-RFA group. In the HR group, there were 13 segmentectomies and 35 wedge resections, with a mean surgical margin of 4.00 mm. In the present study, the average surgical margin of hepatic resection was measured to be 3.81 mm. Post-operative hospital stays were obviously shorter in the HR-plus-RFA group than that in

the HR-alone group [(15.00 ± 4.83) days vs. (21.25 ± 12.21) days, respectively; $p = 0.004$]. The incidence rates of post-operative complications were 15.0% and 25.0%, respectively, in the two groups, but without statistical significance ($p = 0.442$). Two cases (10%) of ileus, 1 case (5%) of pneumonia, 1 case (5%) of bile leakage, 1 case (5%) of anastomosis leakage were reported in the HR-plus-RFA group and 1 case (5.0%) of intraabdominal infection, 1 case (5.0%) of ileus, 1 case (5.0%) of pneumonia were reported in the HR-alone group (Table 2). No surgical mortality occurred in either group.

Survival and recurrence

Median follow-up of all patients was 12.67 months (range 1.87-31.67 months), 15.28 months in the HR-alone group, and 11.78 months in the HR-plus-RFA group (Table 3). In total, 4 patients (4/20, 20%) in the

Table 2. Peri-operative and post-operative features

	HR (N = 20), N (%)	HR + RFA (N = 20), N (%)	<i>p</i> -value
Operative time (minutes)			0.012
Means ± SD	289.40 ± 148.154	194.00 ± 66.243	
Type of hepatic resection			
Segmentectomy	13 (27.08%)	13 (16.46%)	1.000
Wedge resection	35 (72.92%)	66 (83.54%)	0.024
Mean section margin (mm)	4.00	3.71	0.133
Blood loss (ml)			0.243
Means ± SD	657.50 ± 545.86	460.00 ± 506.17	
Transfusion during operation (cases)	13 (65.0%)	11 (55.0%)	0.623
Complication, n (%)	3 (15.0%)	5 (25.0%)	0.442
Abdominal infection	1 (5.0%)	0 (0)	
Ileus	1 (5.0%)	2 (10%)	
Pneumonia	1 (5.0%)	1 (5%)	
Bile leakage	0 (0)	1 (5%)	
Anastomosis leakage	0 (0)	1 (5%)	
Length of hospital stay (days)	21.25 ± 12.21	15.00 ± 4.83	0.040

Table 3. Recurrence and survival

	HR (N = 20), N (%)	HR + RFA (N = 20), N (%)	<i>p</i> -value*
Median follow-up (months) (Q1, Q3)	15.28 (7.35, 22.09)	11.78 (6.30, 18.06)	0.166
Recurrence	20%	65%	0.004
1-year overall survival	90%	80%	0.331
1-year disease-free survival	80%	35%	0.004
1-year cancer-specific survival	90%	85%	0.500

* *p* values were calculated by Fisher exact test.

HR-alone group and 13 patients (13/20, 65%) in the HR-plus-RFA group developed liver recurrence ($p = 0.004$). The HR-alone group had 1-year overall, disease-free and cancer-specific survival rates of 90%, 80%, and 90%, respectively, whereas the HR-plus-RFA group had respective rates of 80%, 35%, and 85% (Table 3, Figs. 2-4). As shown in Table 3, no statistically significant differences were found in 1-year overall survival and cancer-specific survival between the two groups ($p = 0.331$, $p = 0.500$, respectively). The HR-plus-RFA group had significantly inferior

1-year disease-free survival compared to the HR-alone group (35% vs. 80%, $p = 0.004$). Using univariate and multivariate Cox proportional hazards regression analyses of disease-free survival, treatment methods for liver metastasis were found to be independent prognostic factors for tumor recurrence ($p = 0.019$, Table 4).

Discussion

The objective of this study was to compare the

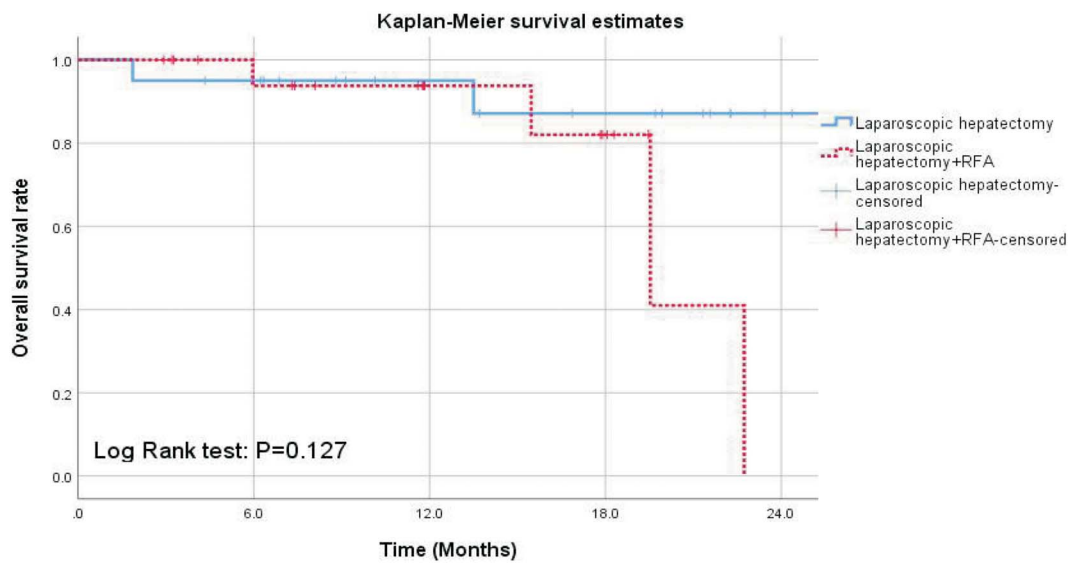


Fig. 2. Kaplan-Meier estimates of 1-year overall survival in the HR and HR versus RFA groups.

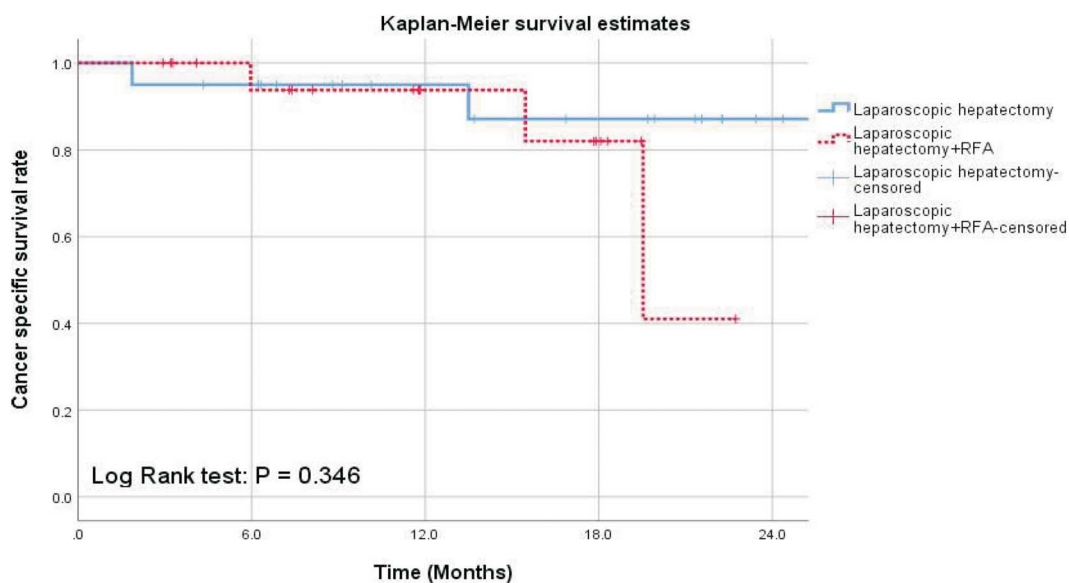


Fig. 3. Kaplan-Meier estimates of 1-year cancer-specific survival in the HR and HR versus RFA groups.

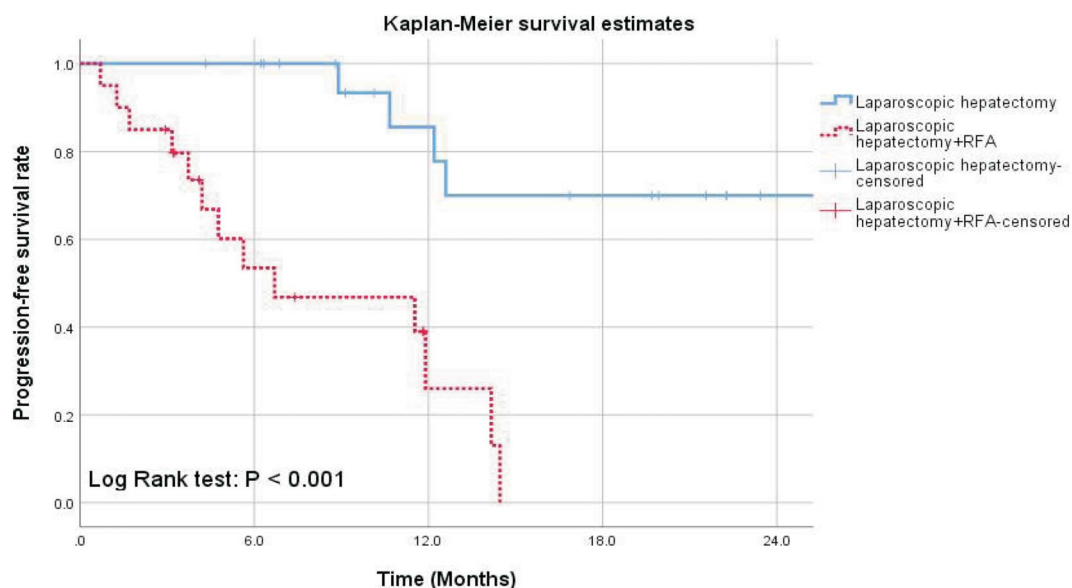


Fig. 4. Kaplan-Meier estimates of 1-year disease-free survival in the HR and HR versus RFA groups.

Table 4. Univariate and multivariate analysis of independent factors associated with 1-year disease-free survival

	Univariate			Multivariate		
	OR	95% CI	<i>p</i> value	OR	95% CI	<i>p</i> value
Age	0.873	0.318-2.398	0.792			
> 60 years old						
≤ 60 years old						
Number of metastases	0.303	0.110-0.835	0.021	0.763	0.223-2.610	0.666
> 3						
≤ 3						
Largest liver tumor (cm)	1.624	0.568-4.643	0.365			
> 3						
≤ 3						
CRLM status						
Multifocality	4.346	0.984-19.196	0.053			
Bilobar involvement	2.731	0.882-8.460	0.082			
Primary tumor location	0.645	0.159-2.623	0.540			
Right						
Left						
Rectum						
Primary T status	0.456	0.147-1.411	0.173			
T1-3						
T4						
PrimaryN status 0	0.365	0.083-1.608	0.183			
1-2						
CEA	0.610	0.224-1.660	0.333			
≥ 10						
< 10						
Treatment HR + RFA	0.122	0.038-0.392	< 0.001	0.152	0.032-0.732	0.019
HR						
Pre-operation chemotherapy	0.298	0.107-0.833	0.021	0.856	0.239-3.064	0.811

short-term prognosis of laparoscopic RFA vs. HR and laparoscopic HR in treatment of CRLMs. Currently, surgical resection is considered to be the best option for curative treatment or long-term survival after CRLM diagnosis. Patients who only receive palliative therapy typically survive just seven to eight months. Survival in liver-resected patients at five years is anywhere between 24% and 40%, with a median survival time of 28-46 months.¹⁷ However, not all patients are ideal candidates for surgical resection. This may be due to the number and location of metastases, instability of the patient, lack of sufficient unaffected liver, or comorbidities. In order to convert an unresectable case to a resectable one, many physicians utilize other treatment regimens in the attempt to reduce tumor size and giving the patient time to qualify as a surgical candidate.

A subcategory of CRC patients has bilobar spread of lesions that require major resection (removal of ≥ 3 anatomical liver segments). The extent of surgery for these patients correlates strongly with an increased risk of acute liver failure as well as complications in the early postoperative period.¹⁸ In these cases, treatment success depends on having a sufficient amount of future liver remnant ranging from at least 30% to 40% of total liver volume.

Taking into account the effectiveness of the surgical method, different surgical strategies have been developed for bilobar forms of CRC. Liver parenchymal-sparing resections achieve similar oncologic outcomes to those of anatomic resections while preserving greater hepatic reserve, which potentially increases salvageability in case of hepatic recurrence. RFA, which has the advantages of minimal invasiveness, and may be favorable for local control of CRLM.¹⁹

Given the advances in imaging-guided location, artificial hydrothorax, and the probes, the indications for RFA have been greatly expanded. In recent years, with the rapid development of local minimally invasive treatment for liver metastases, RFA has been widely applied in the treatment of malignant hepatic tumors, which is safe and minimally invasive, obtaining satisfactory results.²⁰ A new consensus has been reached that RFA can achieve better efficacy in CRC with liver metastasis (diameter < 3 cm and number of metastases ≤ 5) and the liver metastases can be completely

ablated in a better condition (diameter < 5 cm), yielding postoperative 5-year overall survival rates as high as 48%, with an effect comparable to that of surgical resection.²¹ However, the high recurrence rate after RFA has attracted extensive attention, and the application of RFA in the treatment of resectable CRC with liver metastasis is also controversial. The study of Reuter et al.¹¹ showed that the median recurrence time after RFA for liver metastases is shorter than that after surgical resection, and the local recurrence rate and intrahepatic recurrence rate in the RFA group are higher than those in the resection group. Moreover, Aloia et al.²² confirmed in their research on CRC with liver metastasis that surgical resection is superior to RFA in terms of local recurrence and overall survival.

However, in another study on CRC with liver metastasis, the 5-year survival rate and local recurrence rate were similar in patients with lesions < 3 cm after surgery and RFA.²³ In the retrospective study of Lee et al.,²⁴ long-term survival time after RFA was similar to that after surgery in single CRC patients with liver metastasis (≤ 3 cm) or multiple CRC patients with liver metastasis (≤ 2 cm). Also, a recent multicenter randomized prospective trial revealed that thermal ablative therapy as local tumor control improved overall survival (OS) compared to palliative chemotherapy alone in patients with unresectable CRLM.²⁵ Based on this finding, thermal ablative therapy has the potential to be an important treatment option in patients with unresectable CRLM.

In the present study, 90% of patients in the HR-plus-RFA group had multiple liver metastasis in bilobar liver metastases. Therefore, we performed laparoscopic liver resection combined with RFA as a potential opportunity to cure CRC patients with liver metastases, especially those unsuitable for major surgical resection. Three separate approaches are used to perform ablation, including open, laparoscopic, or percutaneous approaches. In our practice, we prefer to perform the laparoscopic approach in lieu of the percutaneous approach because of several noted advantages using laparoscopy. The laparoscopic approach has the benefits of both open and percutaneous approaches. Although it requires general anesthesia and expertise with advanced laparoscopy and ultrasound, the

associated morbidity is much less than that of the open approach.^{26,27} Additionally, the laparoscopic approach has been shown to be superior in terms of local tumor control secondary to precise targeting with laparoscopy and more aggressive ablation with intraoperative ultrasound monitoring.^{28,29} Moreover, thorough examination with laparoscopic ultrasound enables the identification of additional liver tumors that are not seen on preoperative imaging studies. Finally, similar to the open approach, the laparoscopic approach allows better staging for occult peritoneal or hepatic diseases, and effectively treats multiple lesions in the liver with minimal risk of surrounding organ injuries.³⁰ In the present study, no statistically significant differences were seen in the baseline clinical and pathological data between the HR-plus-RFA and the HR-alone groups, while the number of patients with liver metastasis, the percentage of patients receiving neoadjuvant chemotherapy and the extent of liver metastasis (multifocality and bilobar involvement) were significantly higher in the HR-plus-RFA group. Owing to extensive liver disease, RFA combined with surgical resection was considered as the treatment method.

Although the HR-plus-RFA group had significantly more cases with liver metastasis, the operation times and the hospital stays were significantly shorter than those in the HR-alone group. The amount of intraoperative blood loss, blood transfusion and post-operation complications were not significantly different between the two groups. This may be attributed to the unique advantages of RFA in the treatment of CRC with liver metastasis, which helps to avoid and reduce damage to normal liver tissue and adjacent important blood vessels to the greatest degree. In the present series, no statistically significant differences were found between the two surgical groups in postoperative 1-year overall survival and cancer-specific survival. Further analysis of the mortality cases in both groups revealed the following: in the HR-plus-RFA group, there were four mortality cases, three of which were due to tumor recurrence and progression, and the patients refused further surgery and opted for palliative care. The fourth case was a patient who infected with COVID-19 pneumonia and developed septic shock and respiratory failure. In the HR group, there were two

mortality cases, both resulting from tumor recurrence and progression, and the patients declined surgery and sought palliative care. For the aforementioned patient population, undergoing such aggressive and significant surgery, preoperative communication should include the possibility of requiring additional (multiple) surgeries in the event of tumor recurrence postoperatively, in order to achieve better survival. However, the HR-plus-RFA group had a significantly high recurrence rate within one year of treatment and inferior disease-free survival than those in the HR-alone group, basically consistent with reports of previous studies. The tumor recurrence and disease-free survival in CRLM patients are affected by many factors. In the present study, multivariate analyses of disease-free survival showed that the treatment methods for liver metastasis were an independent risk factor for tumor recurrence.

The present study has several limitations. First of all, this study was of retrospective design with the inherent limitation of not being able to generalize results to other populations. However, patients were included consecutively to reduce possible selection bias. Secondly, this study had limited sample size and lacked comprehensive follow-up content. The results presented in this study remain to be verified using multicenter large-sample prospective clinical research in the future. Thirdly, the absence of timely postoperative abdominal computed tomography (CT) follow-up posed challenges in determining the remnant liver volume. However, among all the patients included in this paper, none of them exhibited any symptoms of liver failure. Lastly, ablative therapy and liver resection should not be mutually exclusive, especially in the management of bilobar liver metastases. Concomitant ablative therapy with hepatectomy may spare patients from having two-stage hepatectomy with less morbidity. Newly emerging technology may enable thermal ablation to continue to evolve in patients with resectable and ablatable lesions, in addition to new systemic treatment options, including immunotherapy for metastatic CRC.

Conclusions

When compared to hepatic resection alone for li-

ver metastases in colorectal cancer, surgical resection combined with radiofrequency ablation significantly reduces the operation time and in-hospital stay with a comparable short-term (one-year) survival but the tumor recurrence rate is higher than that in patients receiving hepatic resection alone. More time and effort will be needed in the future to conduct further investigation and research in order to arrive at a rational comprehension about the long-term therapeutic value of the two treatment options.

References

- Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA A Cancer J Clin* 2018;68:394-424. doi: 10.3322/caac.21492.
- Health Promotion Administration, Ministry of Health and Welfare. Taiwan. Cancer Registry Annual Report, 2018.
- Fong Y, Cohen AM, Fortner JG, et al. Liver resection for colorectal metastases. *J Clin Oncol* 1997;15:938-46. doi: 10.1200/JCO.1997.15.3.938.
- Van Cutsem E, Cervantes A, Nordlinger B, et al. Metastatic colorectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2014;25(Suppl. S3):iii1-9. doi: 10.1093/annonc/mdu260.
- Abdalla EK, Vauthey JN, Ellis LM, et al. Recurrence and outcomes following hepatic resection, radiofrequency ablation, and combined resection/ablation for colorectal liver metastases. *Ann Surg* 2004;239:818-25; discussion 825-7.
- Yoo PS, Lopez-Soler RI, Longo WE, et al. Liver resection for metastatic colorectal cancer in the age of neoadjuvant chemotherapy and bevacizumab. *Clin Colorectal Cancer* 2006;6:202-7.
- Tomlinson JS, Jarnagin WR, DeMatteo RP, et al. Actual 10-year survival after resection of colorectal liver metastases defines cure. *J Clin Oncol* 2007;25:4575-80.
- Pawlik TM, Schulick RD, Choti MA. Expanding criteria for resectability of colorectal liver metastases. *Oncologist* 2008;13:51-64.
- Jaffe BM, Donegan WL, Watson F, et al. Factors influencing survival in patients with untreated hepatic metastases. *Surg Gynecol Obstet* 1968;127:1-11.
- Imai K, Allard MA, Castro Benitez C, et al. Long-term outcomes of radiofrequency ablation combined with hepatectomy compared with hepatectomy alone for colorectal liver metastases. *Br J Surg* 2017;104:570-9.
- Reuter NP, Woodall CE, Scoggins CR, et al. Radiofrequency ablation vs. resection for hepatic colorectal metastasis: therapeutically equivalent? *J Gastrointest Surg* 2009;13:486-91.
- Weng M, Zhang Y, Zhou D, et al. Radiofrequency ablation versus resection for colorectal cancer liver metastases: a meta-analysis. *PLoS One* 2012;7:e45493.
- Wu YZ, Li B, Wang T, Wang SJ, et al. Radiofrequency ablation vs hepatic resection for solitary colorectal liver metastasis: a meta-analysis. *World J Gastroenterol* 2011;17:4143-8.
- Therasse P, Arbuck SG, Eisenhauer EA, et al. New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. *J Natl Cancer Inst* 2000;92:205-16.
- deHaas RJ, Wicherts DA, Flores E, et al. R1 resection by necessity for colorectal liver metastases: is it still a contraindication to surgery? *Ann Surg* 2008;248:626-37.
- Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240:205-13.
- Cameron J, Cameron A. Philadelphia: Elsevier Health Sciences; 2016. Current Surgical Therapy E-Book 12th Edition.
- Lafaro K, Buettner S, Maqsood H, et al. Defining post hepatectomy liver insufficiency: where do we stand? *J Gastrointest Surg Off J Soc Surg Alimentary Tract* 2015;19:2079-92.
- Minami Y, Kudo M. Radiofrequency ablation of liver metastases from colorectal cancer: a literature review. *Gut Liver* 2013;7(1):1-6.
- van Amerongen MJ, Jenniskens S, van den Boezem PB, et al. Radiofrequency ablation compared to surgical resection for curative treatment of patients with colorectal liver metastases - a meta-analysis. *HPB (Oxford)* 2017;19:749-56.
- Gillams A, Goldberg N, Ahmed M, et al. Thermal ablation of colorectal liver metastases: a position paper by an international panel of ablation experts, The Interventional Oncology Sans Frontiers Meeting 2013. *Eur Radiol* 2015;25:3438-54.
- Aloia TA, Vauthey JN, Loyer EM, et al. Solitary colorectal liver metastasis: resection determines outcome. *Arch Surg* 2006;141:460-6, 466-7.
- Hur H, Ko YT, Min BS, et al. Comparative study of resection and radiofrequency ablation in the treatment of solitary colorectal liver metastases. *Am J Surg* 2009;197:728-36.
- Lee H, Heo JS, Cho YB, et al. Hepatectomy vs radiofrequency ablation for colorectal liver metastasis: a propensity score analysis. *World J Gastroenterol* 2015;21:3300-7.
- Ruers T, Van Coevorden F, Punt CJ, et al. Local treatment of unresectable colorectal liver metastases: results of a randomized phase II trial. *J Natl Cancer Inst* 2017.
- Gillams A, Goldberg N, Ahmed M, et al. Thermal ablation of colorectal liver metastases: a position paper by an international panel of ablation experts, The Interventional Oncology Sans Frontiers Meeting 2013. *Eur Radiol* 2015;25:3438-54.
- Birsen O, Aliyev S, Aksoy E, et al. A critical analysis of post-operative morbidity and mortality after laparoscopic radiofrequency ablation of liver tumors. *Ann Surg Oncol* 2014;21:1834-40.

28. Berber E, Siperstein A. Local recurrence after laparoscopic radiofrequency ablation of liver tumors: an analysis of 1032 tumors. *Ann Surg Oncol* 2008;15:2757-64.
29. Mulier S, Ruers T, Jamart J, et al. Radiofrequency ablation versus resection for resectable colorectal liver metastases: time for a randomized trial? An update. *Dig Surg* 2008;25:445-60.
30. Sindram D, Lau KN, Martinie JB, et al. Hepatic tumor ablation. *Surg Clin North Am* 2010;90:863-76.

原 著

腹腔鏡射頻消融結合肝切除術治療 結直腸癌肝轉移的短期治療結果

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目的 雖然肝切除術是結直腸癌肝轉移患者的標準局部治療，但目前，射頻消融可能對老年人、小的 (< 3 cm) 孤立病灶、不可切除的病灶或患有慢性病或行動力不佳的弱勢患者扮有治療角色。本研究旨在比較腹腔鏡射頻消融合併肝切除術與腹腔鏡肝切除術治療結直腸癌肝轉移的短期預後。

方法 從 2019 年至 2022 年，在奇美醫學中心有 40 位結直腸癌肝轉移患者分別接受腹腔鏡射頻消融合併肝切除術與腹腔鏡肝切除術治療。這些人分成兩組：20 人接受腹腔鏡射頻消融合併肝切除術，另外 20 人接受腹腔鏡肝切除術。病人臨床統計資料，手術細項，術後結果進行分析。

結果 腹腔鏡射頻消融合併肝切除術與腹腔鏡肝切除術在手術時間和術後住院天數明顯短於腹腔鏡肝切除術。但兩組失血量及輸血袋數沒有統計學上的差異。兩組的短期總體生存率和癌症特異性生存率沒有統計學顯著差異 (分別為 $p = 0.127$ 和 $p = 0.346$)。然而，腹腔鏡射頻消融合併肝切除術與腹腔鏡肝切除術相比，有顯著較差的一年無復發生存率，分別為 35% 和 80% ($p < 0.001$)。單變異與多變異因素分析顯示，腹腔鏡射頻消融合併肝切除術是患者腫瘤復發的獨立危險因子 ($p = 0.019$)。

結論 相較於腹腔鏡肝切除術治療結直腸癌肝轉移患者，接受腹腔鏡射頻消融合併肝切除術明顯地降低手術時間和住院時間，而短期 (一年) 的存活率相當，但腫瘤復發率卻高於僅接受腹腔鏡肝切除術的患者。

關鍵詞 大腸直腸癌、肝臟轉移、肝切除術、射頻消融。