

# World Journal of *Gastrointestinal Oncology*

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WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc.*

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Retrospective Study

## Prognostic factors and therapeutic effects of different treatment modalities for colorectal cancer liver metastases

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### Abstract

#### BACKGROUND

Colorectal cancer (CRC) is one of the most common malignant tumors in China, and the liver is the most common metastatic site in patients with advanced CRC. Hepatectomy is the gold standard treatment for colorectal liver metastases. For patients who cannot undergo radical resection of liver metastases for various reasons, ablation therapy, interventional therapy, and systemic chemotherapy can be used to improve their quality of life and prolong their survival time.

#### AIM

To explore the prognostic factors and treatments of liver metastases of CRC.

#### METHODS

A retrospective analysis was conducted on 87 patients with liver metastases from CRC treated at the Liaoning Cancer Hospital and Institute between January 2005 and March 2011. According to different treatments, the patients were divided into the following four groups: Surgical resection group (36 patients); ablation group (23 patients); intervention group (15 patients); and drug group (13 patients). The clinicopathological data and postoperative survival of the four groups were analyzed. The Kaplan-Meier method was used for survival analysis, and the Cox proportional hazards regression model was used for multivariate analysis.

Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

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## RESULTS

The median survival time of the 87 patients was  $38.747 \pm 3.062$  mo, and the 1- and 3-year survival rates were 87.5% and 53.1%, respectively. The Cox proportional hazards model showed that the following factors were independent factors affecting prognosis: The degree of tumor differentiation, the number of metastases, the size of metastases, and whether the metastases are close to great vessels. The results of treatment factor analysis showed that the effect of surgical treatment was better than that of drugs, intervention, or ablation alone, and the median survival time was  $48.83 \pm 4.36$  mo. The drug group had the worst prognosis, with a median survival time of only  $13.5 \pm 0.7$  mo ( $P < 0.05$ ). For patients with liver metastases of CRC near the great vessels, the median survival time (27.3 mo) of patients undergoing surgical resection was better than that of patients using other treatments (20.6 mo) ( $P < 0.05$ ).

## CONCLUSION

Patients with a low degree of primary tumor differentiation, multiple liver metastases (number of tumors  $> 4$ ), and maximum diameter of liver metastases  $> 5$  cm have a poor prognosis. Among drug therapy, intervention, ablation, and surgical treatment options, surgical treatment is the first choice for liver metastases. When liver metastases are close to great vessels, surgical treatment is significantly better than drug therapy, intervention, and ablation alone.

**Key Words:** Colorectal cancer; Liver metastasis; Prognostic factors; Ablation; Surgical resection; Retrospective study

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**Core Tip:** Pathological data of patients with liver metastases from colorectal cancer were analyzed and the diameter, differentiation, and multiple lesions of liver metastases, were found to indicate a poor prognosis. The analysis of different treatment methods for patients with liver metastases from colorectal cancer proved that radical surgery is always the best option. For inoperable patients, personalized combination therapy is actively recommended.

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## INTRODUCTION

Colorectal cancer (CRC) is one of the most common malignant tumors in China, and its mortality has been increasing in recent years, ranking fourth in the incidence of malignant tumors, and the incidence increases with age<sup>[1,2]</sup>. The liver is the most common metastatic site in patients with advanced CRC. More than 50% of patients with CRC may develop colorectal liver metastases (CLMs), and approximately 20% of these patients have liver metastases at the initial diagnosis<sup>[3,4]</sup>. Hepatectomy is the gold standard treatment for CLM, with a 5-year overall survival rate of 58%<sup>[5,6]</sup>. However, 80% to 85% of patients with advanced CLM are still unable to achieve R0 resection<sup>[7-9]</sup>. For patients who cannot undergo radical resection of liver metastases for various reasons, ablation therapy, interventional therapy, and systemic chemotherapy can be used to improve their quality of life and prolong their survival time. In this study, we collected the data from 87 patients with CLM and compared their prognostic factors and treatments, with the hope of obtaining a more reasonable treatment plan and provide evidence for clinical treatment.



## MATERIALS AND METHODS

### **Clinical information**

The data of 103 patients with CLM treated at the Departments of Hepatobiliary Surgery, Colorectal Surgery and Intervention of the Liaoning Cancer Hospital and Institute between January 2005 and March 2011 were collected. Patients with incomplete follow-up were excluded; a total of 87 patients were included, including 61 males and 26 females. According to different treatments for liver metastases, the patients with CLM were divided into four groups: Surgical resection group (36 patients); ablation group (23 patients); intervention group (15 patients); and drug group (13 patients). The inclusion criteria were as follows: (1) Patients with a clear pathological diagnosis of CRC accompanied by liver metastasis; (2) Patients who underwent radical surgery for the primary lesion (open or laparoscopic); (3) Patients who agreed to receive different treatment plans, which were discussed by the multidisciplinary diagnosis and treatment (MDT) team; (4) Patients who could be divided into two groups according to the distance between CLM and great vessels: Those near great vessels and those not near; (5) Patients who received FOLFOX or CapeOx (XELOX) chemotherapy or other biological targeted therapy; and (6) Patients whose interventional therapy was transcatheter arterial chemoembolization (TACE), and the chemotherapy drugs infused were calcium folinate and pentafluorouracil. The exclusion criteria were as follows: (1) Patients with communication difficulties; and (2) Patients who did not cooperate with this study. This study was approved by the Ethics Committee of the hospital. The data are anonymous, and the requirement for informed consent was therefore waived.

### **Selection of clinicopathological factors**

The following clinicopathological factors were selected for analysis: Sex, age, primary tumor size, primary tumor site, pathological type, degree of differentiation, carcinoembryonic antigen (CEA), cancer antigen (CA) 19-9, lymph node metastasis, distribution of CLMs, number of CLMs, proximity to great vessels, diameter of the largest CLM, postoperative chemotherapy cycle, *etc.* Among them,  $\leq 1$  cm was used to define whether the CLM is close to a great vessel. The great vessels include the intrahepatic portal vein trunk and secondary and tertiary branches, the left hepatic, right hepatic, and middle hepatic veins, and the vena cava.

### **Evaluation indicators**

The following indicators were used to evaluate the short-term effects: Indicators of liver function tests; Perioperative complications and adverse drug reactions during the treatment period; and Physical evaluation (physical condition scores were rated according to the Eastern Cooperative Oncology Group score standard).

The following indicators were used to evaluate the long-term efficacy: Recurrent-free survival (RFS); Tumor remission assessment (according to the Response Evaluation Criteria in Solid Tumours criteria).

### **Follow-up**

Follow-up was performed by telephone and outpatient review. The follow-up deadline was January 1, 2015, and the median follow-up time was 20.8 mo. A total of 16 patients were lost to follow-up in this group, and the follow-up rate was 83.5%. The recorded survival time was from the time of surgery to the time of the last follow-up, death, or the deadline of follow-up (including loss to follow-up, death from other diseases, *etc.*).

### **Statistical analysis**

SPSS 22.0 software was used for statistical analyses. Measurement data are expressed as the mean  $\pm$  SD. The comparison between groups was analyzed by single factor analysis of variance. The unevenness of variance was measured by the Kruskal-Wallis test. Comparisons between groups were made using the  $\chi^2$  test or continuous correction. Kaplan-Meier survival curves were used to indicate the RFS. The log-rank test was used for comparisons between the two groups. Significant single factors were incorporated into the Cox regression equation for multifactor analysis.

## RESULTS

### **Comparison of case data among the four groups**

In the comparison of clinicopathological data, there was no significant difference in the four groups of patients in terms of sex, primary tumor size, primary tumor location, pathological type, degree of differentiation, CEA, CA19-9, lymph node metastasis, and total chemotherapy time. More older patients were in the drug group and intervention group, but there was no significant difference. There were significant differences in the distribution of CLM, the diameter of the largest CLM, and the distance to great vessels ( $P < 0.05$ , Table 1).

### **Comparison of complications**

None of the patients in the four groups died within 1 mo. The common symptoms were fever, pain in the liver area, and abnormal liver function. All patients recovered after symptomatic treatment. Of the 36 patients in the surgical resection group, four (11.1%) had postoperative complications, including two cases of postoperative liver wound bleeding, which were cured after symptomatic conservative treatment of hemostasis, and two cases of incision infection and dehiscence, which were cured by conservative treatment. None of the patients were treated by secondary surgery. There were no other definite complications or adverse reactions caused by drugs in the other three groups. Patients in the surgical resection group had abnormal liver function during the perioperative period, which improved after symptomatic liver protection treatment.

### **Survival**

The median survival time of the 87 patients was  $38.747 \pm 3.062$  mo, and the 1- and 3-year survival rates were 87.5% and 53.1%, respectively.

### **Prognostic univariate and multivariate analyses**

**Univariate analysis:** The analysis of prognostic factors for the overall survival of patients with CLM showed that the following six factors were statistically significant for prognosis ( $P < 0.05$ ): Degree of pathological differentiation, CEA, number of CLMs, diameter of maximum CLM, treatment of CLM, and proximity to great vessels or not (Table 2).

**Multivariate analysis:** The significant factors ( $P < 0.05$ ) in the univariate prognostic analysis were incorporated into the multivariate Cox regression model, and the following results were obtained: The degree of tumor differentiation, the number of metastases, the size of metastases, and the proximity to great vessels were independent factors affecting the prognosis of CLM ( $P < 0.05$ , Table 3).

**Survival curve analysis:** Patients with a high degree of differentiation of the primary tumor had a better prognosis than those with a low degree of differentiation ( $P < 0.05$ , Figure 1A). Patients with the number of CLM  $\leq 4$  had better RFS than patients with the number of CLM  $> 4$  ( $P < 0.05$ , Figure 1B). At the same time, the survival curves of the two groups of patients flattened after 2 years of diagnosis. The RFS of patients with a liver metastasis with a maximum diameter  $\leq 5$  cm was significantly better than that of patients with a diameter  $> 5$  cm ( $P < 0.05$ , Figure 1C).

### **Analysis of treatment factors**

An analysis was performed on the 87 patients. Among the patients, there were 13 patients in the drug group, 23 in the ablation group, 15 in the intervention group, and 36 in the surgical resection group. The results showed that patients who underwent surgical treatment had better RFS than patients who underwent interventional therapy, ablation therapy, or drug therapy. The median survival time in the surgical resection group was  $48.83 \pm 4.36$  mo; the drug group had the worst prognosis, with a median survival time of only  $13.5 \pm 0.7$  mo (Figure 2).

### **Analysis of whether liver metastasis is close to great vessels**

A separate group comparison analysis was performed on whether the intrahepatic metastases were close to great vessels. The results showed that there were no significant differences in the general clinicopathological characteristics between the two groups, but there were differences in the treatments. Among patients with tumors close to great vessels, five chose surgical resection, ten chose interventional therapy, two chose ablation therapy, and only one selected drug therapy (Table 4).



Table 1 Comparison of clinicopathological data of the four groups of patients

	Drug	Ablation	Intervention	Surgical resection	Statistical value	P value
Gender					$\chi^2 = 2.459$	0.483
Male	8	19	10	24		
Female	5	4	5	12		
Age (yr)	62.77 ± 8.55	60.39 ± 9.33	63.13 ± 10.57	57.50 ± 12.52	F = 1.337	0.268
Primary tumor size (cm)	5.08 ± 2.17	4.35 ± 1.40	5.37 ± 2.72	5.10 ± 2.06	F = 0.940	0.425
Primary tumor site					$\chi^2 = 11.729$	0.068
Right colon	6	6	3	7		
Left colon	5	4	3	16		
Rectum	2	13	9	13		
Pathological type					$\chi^2 = 3.032$	0.387
Non-MUC	11	20	11	33		
MUC	2	3	4	3		
Differentiation					$\chi^2 = 7.807$	0.253
High	4	4	1	10		
Moderate	7	13	8	22		
Low	2	6	6	4		
CEA (ng/mL)					$\chi^2 = 2.950$	0.339
≤ 15	11	13	10	24		
> 15	2	10	5	12		
CA19-9 (U/mL)					$\chi^2 = 0.576$	0.902
≤ 37	10	15	10	25		
> 37	3	8	5	11		
LMN					$\chi^2 = 4.346$	0.226
No	6	14	7	12		
Yes	7	9	8	24		
CLM distribution					$\chi^2 = 17.169$	0.009
Right lobe	4	15	4	14		
Left lobe	5	0	1	5		
Both lobes	4	8	10	17		
CLM number					$\chi^2 = 5.051$	0.168
≤ 4	8	16	5	21		
> 4	5	7	10	15		
Proximity to great vessels					$\chi^2 = 23.693$	0.000
No	12	21	5	31		
Yes	1	2	10	5		
Maximum CLM diameter (cm)	4.96 ± 2.81	4.72 ± 1.74	5.03 ± 1.39	2.93 ± 1.11	F = 9.627	0.000
Total chemotherapy time					$\chi^2 = 5.729$	0.126
< 6 mo	13	18	14	27		
≥ 6 mo	0	5	1	9		

MUC: Mucinous colorectal adenocarcinomas; CEA: Carcinoembryonic antigen; CA19-9: Cancer antigen 19-9; LMN: Lymph node metastases; CLM:

According to our analysis of the 18 patients with CLM near great vessels, the median survival time (27.3 mo) of patients undergoing surgery was significantly better than that (20.6 mo) of patients receiving other treatments ( $P < 0.05$ , Figure 3).

## DISCUSSION

The liver is a common site of hematogenous metastases in CRC. Approximately 30%-50% of patients with CRC develop simultaneous or metachronous CLM. Liver metastasis has become one of the leading causes of death in patients with CRC<sup>[10-15]</sup>. The MDT team conducted a comprehensive evaluation of patients with CLM, individually formulated treatment plans, carried out corresponding comprehensive treatments, and improved the 5-year survival rate<sup>[16]</sup>. Therefore, in order to establish more reasonable treatment plans, the clinical data of 87 patients with CLM who were treated by surgical resection, ablation, interventional therapy, and medicine alone were analyzed, their survival was followed, and prognostic factors and treatments were compared.

The results showed that there were no significant differences in sex, primary focus size, primary focus site, pathological type, degree of differentiation, CEA, CA19-9, lymph node metastasis, or total chemotherapy time in the four groups of patients, indicating that there was no special preference in the patient's general status. However, patients who chose drug therapy and interventional therapy were older. The reason may be related to the patient's comprehensive state and treatment expectations. Some patients and their families were unwilling to bear the risk of surgery and refuse to undergo surgical treatment. Many previous studies have shown that the lower the degree of differentiation of the primary tumor (mainly manifested by more aggressive and malignant phenotype), the worse the prognosis; the number of metastases ( $\leq 4$ ) and the diameter of metastases ( $\leq 5$  cm) are the main prognostic factors affecting the prognosis of patients with CLM<sup>[17-19]</sup>. This study also analyzed the degree of differentiation, the number of CLMs, and the maximum diameter of metastases and obtained similar results. In summary, the lower the degree of tumor differentiation, the greater the number of metastases, and the larger the diameter of the metastases, the heavier the tumor burden will be throughout the body, and the shorter the survival period. In addition, the distance between metastases and great vessels also affected the recurrent-free survival of patients. With  $\leq 1$  cm as the boundary, patients with metastases near great vessels had a worse prognosis than patients with metastases far from great vessels, which is related to the rich blood flow that may be beneficial to tumor invasion and metastasis.

The median survival time of patients with unresectable intrahepatic metastases is less than 12 mo<sup>[20]</sup>. For patients with resectable CLM, the 5-year survival rate of those who choose radical resection is between 38% and 58%<sup>[21,22]</sup>, and the benefits are obvious. We found that the following three factors determined the possibility of radical resection: The distribution of CLMs, the diameter of the largest CLM, and the distance to great vessels. We temporarily defined patients with CLMs that could not be resected at one stage as potentially resectable patients. Some of the initially unresectable patients could be converted into resectable patients through local or systemic chemotherapy and other treatments<sup>[23-25]</sup>. Patients were treated by short-course radiotherapy and upfront chemotherapy, with delayed surgery<sup>[26,27]</sup>. Upfront systemic chemotherapy can reduce the size of primary lesion and metastasis, and the extent of surgery<sup>[28]</sup>. Compared with other treatments, the advantage of surgical resection is that it can remove all visible tumors in the liver and can reach R0 resection. Radical resection was achieved in all selected patients in this study (Figure 4). In addition, the widespread use of ultrasound in surgery can improve the rate of intraoperative exploration. For metastatic lesions not found before surgery, ultrasound can help to locate the lesion and provide a more reasonable surgical treatment in a timely manner to avoid residual tumors and improve the rate of R0 resection<sup>[29,30]</sup>. For all selected patients in this study, intraoperative ultrasound localization was used (Figures 5 and 6) to ensure R0 resection.

In addition to surgical resection for CLM, ablation, intervention, and chemotherapy alone (and/or a combination of targeted drugs) have been widely used clinically. In addition, new liver exploration and treatment methods are constantly emerging<sup>[31-37]</sup>.

Table 2 Single factor analysis of prognosis of the patients

Variable	n	Recurrent-free survival (%)		$\chi^2$	P value
		1 yr	3 yr		
Gender				0.977	0.323
Male	61	91.4	55.9		
Female	26	78.3	46.5		
Age (yr)				0.509	0.475
≤ 60	50	82.7	49.6		
> 60	37	94.2	57.4		
Primary tumor size (cm)				0.006	0.937
≤ 5	66	87.1	56.2		
> 5	21	89.5	46.4		
Primary tumor site				5.365	0.068
Right colon	22	85.2	38.8		
Left colon	37	83.2	47.3		
Rectum	28	96.0	75.1		
Differentiation				9.228	0.010
High	19	83.9	77.9		
Moderate	50	93.2	55.4		
Low	18	76.5	29.4		
Pathological type				0.000	0.987
Non-MUC	75	88.4	51.2		
MUC	12	83.3	64.3		
CEA (ng/mL)				5.636	0.018
≤ 15	58	92.3	65.2		
> 15	29	85.8	20.2		
CA199 (U/mL)				0.029	0.866
≤ 37	60	92.3	55.0		
> 37	27	85.5	52.2		
LMN				0.385	0.535
No	39	91.2	55.3		
Yes	48	83.2	51.3		
CLM distribution				1.036	0.596
Right lobe	37	82.5	53.9		
Left lobe	11	90.9	56.6		
Both lobes	39	91.6	52.7		
CLM number				4.152	0.042
≤ 4	50	90.7	59.6		
> 4	37	91.4	29.1		
Maximum CLM diameter				10.732	0.001
≤ 5 cm	65	93.2	61.4		
> 5 cm	22	85.2	18.7		
CLM treatments				8.158	0.043

Drug	13	90.9	51.9		
Ablation	23	72.5	37.5		
Intervention	15	92.3	34.6		
Surgical resection	36	96.8	61.9		
Proximity to great vessels				4.412	0.036
No	69	90.5	59.6		
Yes	18	77.4	36.1		
Postoperative chemotherapy time				0.367	0.545
≤ 6 mo	72	79.4	42.8		
> 6 mo	15	89.5	56.3		

MUC: Mucinous colorectal adenocarcinomas; CEA: Carcinoembryonic antigen; CA19-9: Cancer antigen 19-9; LMN: Lymph node metastases; CLM: Colorectal liver metastases.

However, our study showed that the median survival time of patients who underwent surgical treatment was the longest, reaching  $48.83 \pm 4.36$  mo, which was significantly better than that of intervention, ablation (Figure 7), and drug therapy. Therefore, the preferred treatment for patients with CLM is still surgery. Especially when the metastases are close to great vessels, surgical treatment has a greater benefit. Among the patients enrolled in this study, it is important to point out that of the 15 patients with CLM close to great vessels treated by ablation, eight had tumor recurrence *in situ* within 6 mo after surgery. The ablation effect of the metastasis near great vessels is not satisfactory. This may be due to the heat sink effect; that is, the blood vessels in the liver take away some of the heat from the thermal ablation zone, which will cause local cooling and prevent complete ablation<sup>[38,39]</sup>. Existing studies have suggested that ablation treatment can effectively treat CLM, especially when the metastasis is  $\leq 3$  cm; however, when the lesion is larger than 5 cm, it is difficult to achieve complete necrosis using ablation treatment. Complications may be more frequent when the lesion is located near the submental or portal or inferior vena cava<sup>[40-42]</sup>. In addition, incomplete tumor ablation still exists within a distance of 1 cm between the great vessels in the liver and the ablation electrode, which may have a significant impact on the local tumor recurrence rate<sup>[43]</sup>. Previous studies have shown that for some patients who are initially unresectable, surgery combined with ablation may be a safe and effective potential alternative after effective chemotherapy<sup>[44]</sup>.

The efficacy of intervention alone for CLM is limited, and this study showed that the RFS of patients after intervention cannot be compared with that after surgical resection. The reason is that in addition to the hepatic arteries, the main source of blood supply for intrahepatic metastases in CLM patients is the portal vein. Because the portal vein branch of the blood supply to the liver tumor cannot be embolized, the treatment effect cannot be compared with the treatment effect for liver cancer dominated by a hepatic artery blood supply. However, most researchers believe that TACE treatment can significantly control tumor growth locally, shrink tumors, and increase the chance of surgical resection. At the same time, compared with simple drug therapy, during TACE treatment, the concentration of cytotoxic drugs in CLM is significantly increased and the systemic toxicity is small, which is more suitable for potentially resectable patients<sup>[45,46]</sup>. However, our experience suggests that after TACE treatment, CLMs will have different degrees of adhesion to the abdominal wall and diaphragm, which will increase the difficulty of surgical R0 resection and the incidence of postoperative complications. The reason for this may be the liver inflammation caused by liver tumors treated with TACE and the drug response caused by the high concentration of chemotherapy drug perfusion. Therefore, we believe that TACE treatment is relatively limited for CLM patients with potential surgical resection and is more suitable for the local treatment of tumors in unresectable patients. Nevertheless, some studies have shown that with a tumor diameter less than 3 cm, the long-term survival rate of patients treated with combined ablation is significantly better than that of patients treated with monotherapy, and the treatment effect is significantly improved compared with monotherapy<sup>[47,48]</sup>.

In some other patients, drug therapy is often used when the above treatments cannot be performed for various reasons. Patients in the drug therapy group received XELOX chemotherapy or other biological targeted therapy, without any invasive

Table 3 Multifactor analysis

Variable	B	SE	Wald	df	Sig.	Exp(B)
Step 1						
Differentiation			4.174	2	0.124	
Differentiation (1)	-0.865	0.590	2.148	1	0.143	0.421
Differentiation (2)	-0.763	0.406	3.528	1	0.060	0.466
CEA classification	0.076	0.434	0.030	1	0.861	1.079
Number of metastases	-0.758	0.416	3.323	1	0.068	0.468
Size of metastases	1.516	0.396	14.616	1	0.000	4.552
Proximity to great vessels	-0.794	0.417	3.616	1	0.057	0.452
Liver treatment	-0.094	0.174	0.288	1	0.591	0.911
Step 2						
Differentiation			4.173	2	0.124	
Differentiation (1)	-0.860	0.589	2.133	1	0.144	0.423
Differentiation (2)	-0.749	0.398	3.532	1	0.060	0.473
Number of metastases	-0.754	0.414	3.312	1	0.069	0.471
Size of metastases	1.526	0.392	15.190	1	0.000	4.599
Proximity to great vessels	-0.797	0.417	3.656	1	0.056	0.451
Liver treatment	-0.097	0.174	0.308	1	0.579	0.908
Step 3						
Differentiation			4.373	2	0.112	
Differentiation (1)	-0.839	0.585	2.057	1	0.151	0.432
Differentiation (2)	-0.776	0.396	3.834	1	0.050	0.460
Number of metastases	-0.795	0.409	3.778	1	0.052	0.451
Size of metastases	1.583	0.379	17.438	1	0.000	4.870
Proximity to great vessels	-0.793	0.416	3.639	1	0.056	0.452
Step 4						
Number of metastases	-0.910	0.405	5.065	1	0.024	0.402
Size of metastases	1.490	0.366	16.596	1	0.000	4.438
Proximity to great vessels	-1.001	0.396	6.384	1	0.012	0.367
Differentiation	1.384	0.392	7.238	1	0.008	0.507

treatment. Only one case was treated with chemotherapy combined with targeted therapy (bevacizumab). Since fewer patients are treated with targeted therapy, the prognosis of targeted therapy is not discussed. The results of our study showed that the median survival time with drug therapy was only  $13.5 \pm 0.7$  mo, which is far inferior to that of surgical treatment. At present, the targeted therapeutic drugs for CLM mainly include monoclonal antibodies against EGFR and VEGF. At present, cetuximab and bevacizumab are commonly used in China. Most guidelines recommend the use of a fluorouracil-based chemotherapy combined with oxycotin<sup>[49]</sup>. Other studies have also shown that the combination of intervention and systemic chemotherapy or targeted therapy is an effective treatment option that allows patients to be completely resected and have a good prognosis<sup>[50-52]</sup>. Therefore, for patients who cannot undergo radical resection, combined treatment seems more appropriate, but the actual condition and the patient's own wishes need to be considered<sup>[53]</sup>.

**Table 4 Comparison of clinicopathology between not-near great vessel group (A) and near great vessel group (B)**

	A	B	Statistics	P value
Gender			$\chi^2 = 0.048$	0.826
Male	48	13		
Female	21	5		
Age (yr)	59.22 ± 10.34	63.11 ± 12.90	t = 1.350	0.181
Primary tumor size (cm)	4.73 ± 1.84	5.75 ± 2.65	t = 1.900	0.061
Primary tumor site			$\chi^2 = 0.519$	0.771
Right colon	18	4		
Left colon	23	5		
Rectum	28	9		
Pathological type			$\chi^2 = 0.456$	0.500
Non-MUC	60	15		
MUC	19	3		
Differentiation			$\chi^2 = 4.581$	0.101
High	16	3		
Medium	42	8		
Low	11	7		
CEA (ng/mL)			$\chi^2 = 0.315$	0.574
≤ 15	45	13		
> 15	24	5		
CA19-9 (U/mL)			$\chi^2 = 0.654$	0.419
≤ 37	49	11		
> 37	20	7		
LMN			$\chi^2 = 0.001$	0.971
No	31	8		
Yes	38	10		
CLM distribution			$\chi^2 = 2.546$	0.280
Right lobe	32	5		
Left lobe	9	2		
Both lobes	28	11		
CLM number			$\chi^2 = 3.206$	0.073
≤ 4	43	7		
> 4	26	11		
Maximum CLM diameter (cm)	4.04 ± 1.97	4.19 ± 1.69	t = 0.309	0.758
Postoperative chemotherapy time			$\chi^2 = 1.766$	0.184
≤ 6 mo	59	13		
> 6 mo	10	5		
CLM treatments			$\chi^2 = 23.693$	0.000
Drug	12	1		
Ablation	21	2		
Intervention	5	10		
Surgical resection	31	5		



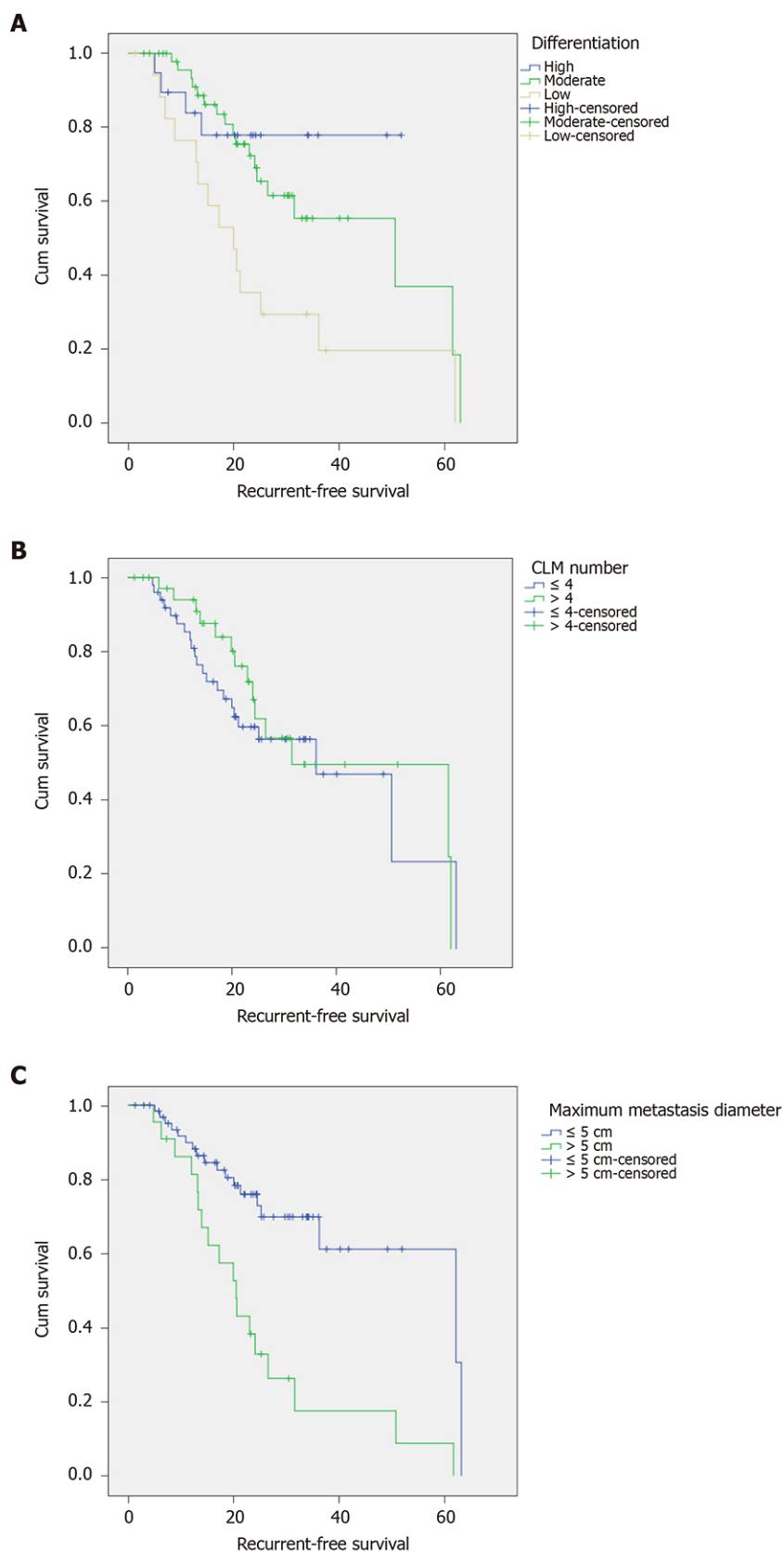
MUC: Mucinous colorectal adenocarcinomas; CEA: Carcinoembryonic antigen; CA19-9: Cancer antigen 19-9; LMN: Lymph node metastases; CLM: Colorectal liver metastases.

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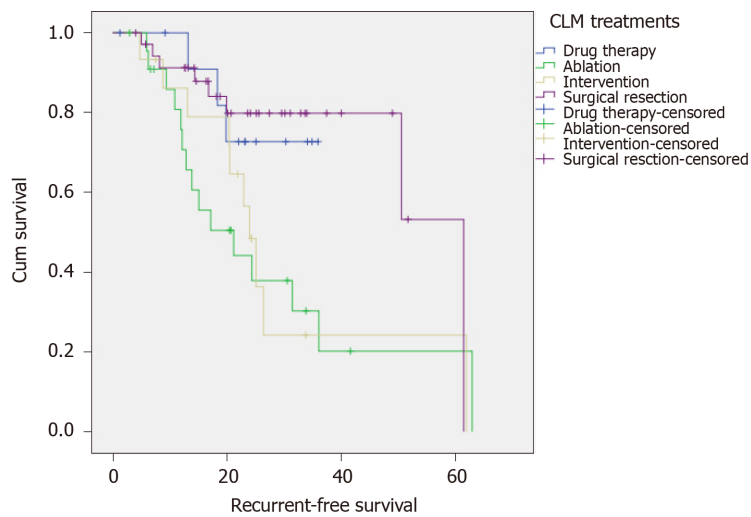
## CONCLUSION

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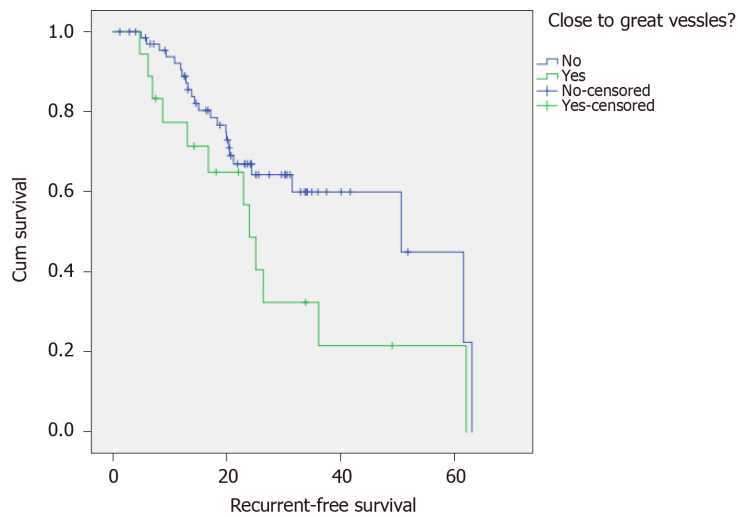
In summary, in the treatment of patients with CLM, radical surgery is still the main method. However, the treatment should be carried out by a MDT team based on the actual condition of the patient, comprehensively identifying their adverse prognostic factors, correctly assessing the general state of the patient, and formulating the best treatment plan to ensure maximum benefit for the patient. The limitation of this study is that it was retrospective, and some index samples were small in the group comparison. Therefore, it is necessary to expand the sample size and provide evidence-based evidence for the treatment of CLM through multidisciplinary communication or further prospective research.



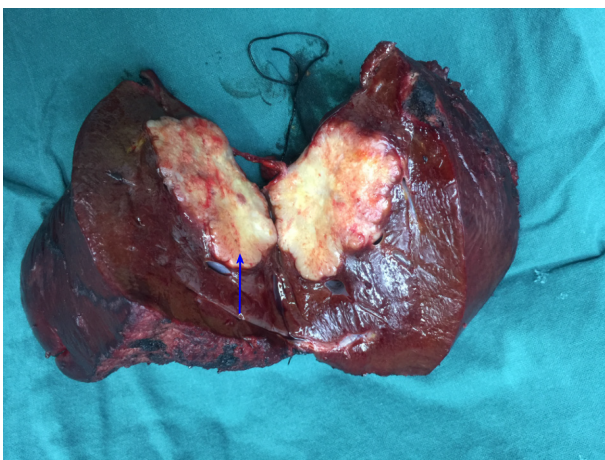
**Figure 1 Survival curves of patients.** A: Different differentiation degrees of the primary tumor; B: Colorectal liver metastases  $\leq 4$  and  $> 4$ ; C: Colorectal liver metastases with a maximum metastasis diameter of  $\leq 5$  cm and  $> 5$  cm. CLM: Colorectal liver metastases.



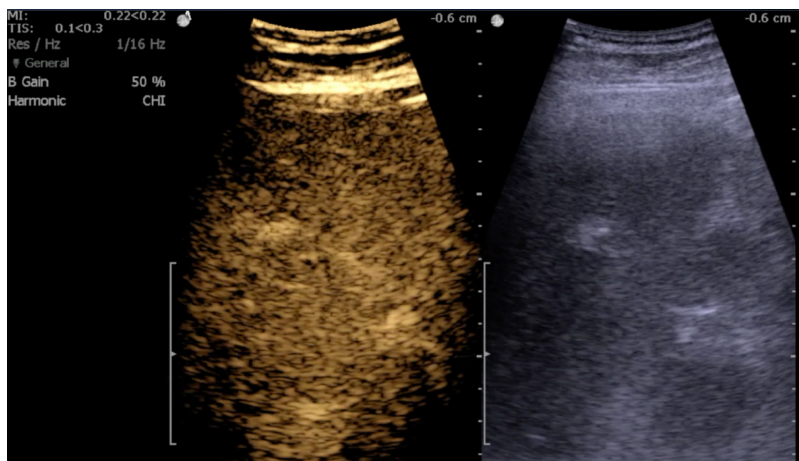
**Figure 2** Survival curves for different treatments. CLM: Colorectal liver metastases.



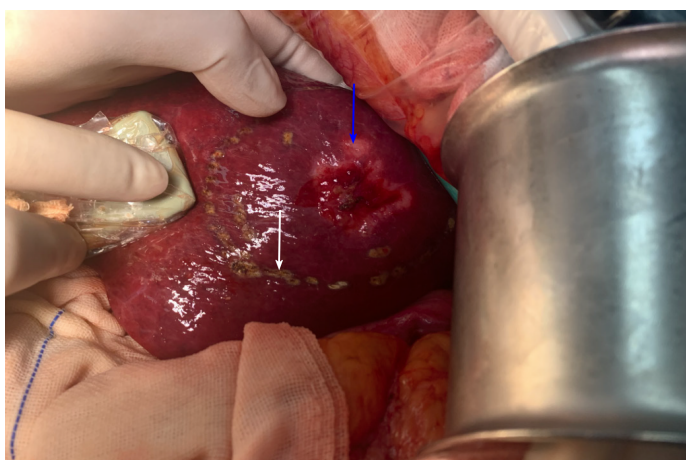
**Figure 3** Survival curves of colorectal liver metastases near or not near great vessels.



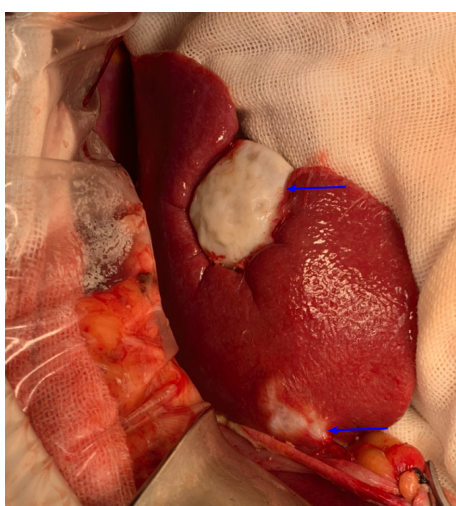
**Figure 4** Surgical resection of colorectal liver metastases. The arrow indicates metastases.



**Figure 5** Intraoperative ultrasound positioning.



**Figure 6** Intraoperative ultrasound localization. Blue arrow represents colorectal liver metastases, and white arrow represents electrosurgical markers after ultrasound localization.



**Figure 7** Radiofrequency ablation. Arrows indicate necrosis of colorectal liver metastases.

## ARTICLE HIGHLIGHTS

**Research background**

Methods such as hepatectomy, ablation therapy, interventional therapy, and systemic chemotherapy improve the quality of life and prolong survival. Through the comparison of different prognostic factors and treatment plans, it is hoped that a more reasonable treatment plan will be obtained, which will provide evidence-based basis for clinical treatment.

**Research motivation**

This study analyzed the prognosis of different treatment methods, combining pathological characteristics and prognostic factors to formulate the most suitable treatment plan for patients.

**Research objective**

Through the comparison of prognostic factors and treatment rules, it is hoped that a more reasonable treatment plan will be obtained, which will provide evidence-based basis for clinical treatment.

**Research methods**

The clinicopathological data and postoperative survival of four groups of colorectal cancer patients with liver metastases (surgical resection group, ablation treatment group, interventional treatment group, and chemotherapy alone group) were retrospectively analyzed. The survival analysis was performed by the Kaplan-Meier method, and multivariate Cox proportional hazard regression model was used for analysis.

**Research results**

The Cox proportional hazards model showed that the following factors are independent factors affecting prognosis: The degree of tumor differentiation, the number of metastases, the size of metastases, and whether the metastases are close to great vessels. The effect of surgical treatment was better than that of drugs, intervention, or ablation alone.

**Research conclusions**

Patients with a low degree of primary tumor differentiation, multiple liver metastases (number of tumors > 4), and maximum diameter of liver metastases > 5 cm have a poor prognosis. Surgical treatment is the first choice for liver metastases, especially when liver metastases are close to great vessels.

**Research perspectives**

Radical surgery is the first choice for the treatment of patients with liver metastases from colorectal cancer. At the same time, multidisciplinary diagnosis and treatment should be discussed and combined with the actual situation to develop the most suitable treatment plan for the patient.

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