Prognostic value of carcinoembryonic antigen level in patients with colorectal cancer liver metastasis treated with percutaneous microwave ablation under ultrasound guidance

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Abstract  
Thermal ablation is an alternative treatment for colorectal cancer liver metastasis (CRLM). However, prognostic factors in patients with CRLM who have undergone microwave ablation (MWA) have not been clearly defined. Therefore, this study aimed to analyze the risk factors associated with early recurrence in patients with CRLM treated with MWA.  
Herein, we retrospectively analyzed data for 140 patients with CRLM who underwent MWA from 2013 to 2015 in our institution. Patients were grouped by median pretreatment carcinoembryonic antigen (CEA) level into the high CEA level (≥3.7 ng/mL) group and low CEA level (<3.7 ng/mL) group. Variables that might affect overall survival were subjected to univariable and multivariable Cox regression analysis.  
Our results showed a median progression-free survival (PFS) and median liver progression-free survival (LPFS) of 9 and 11.5 months, respectively, for the 99 CRLM patients analyzed. Both the median PFS duration (7.5 vs. 12.0 months; hazard ratio [HR]: 1.852; 95% confidence interval [CI]: 1.131–3.034; P = .014) and LPFS duration (7.5 vs 14.0 months; HR: 2.117; 95% CI: 1.247–3.593; P = .005) were significantly shorter in the high CEA level group than in the low level group. In multivariable analysis, high CEA level, >3 tumors, and positive node status for the primary tumor were independent factors for PFS, with corrected HRs of 2.11 (95% CI: 1.257–3.555; P = .005), 2.450 (95% CI: 1.420–4.226; P = .001), and 2.265 (95% CI: 1.304–3.935; P = .004), respectively. However, age, tumor size, regional lymph node were not associated with LPFS.  
CEA level could be a valuable prognostic factor for early recurrence in patients with CRLM after MWA irrespective of the presence of early local recurrence in the liver or disease progression.  

Abbreviations: CEA = carcinoembryonic antigen, CEUS = contrast-enhanced, CRLM = colorectal cancer liver metastasis, EGFR = epidermal growth factor receptor, LPFS = liver progression-free survival, MDT = multi-disciplinary team, MWA = microwave ablation, OS = overall survival, PFS = progression-free survival.

Keywords: carcinoembryonic antigen value, colorectal cancer, disease progression, liver metastasis, liver progression, microwave ablation

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1. Introduction

Colorectal cancer is one of the most common cancers and the leading cause of death worldwide; liver metastases occur in up to 60% of colorectal cancer patients.\(^1\) The liver is the most common site of metastasis in colorectal cancer and is detected in nearly 25% of patients at initial diagnosis and 50% to 70% of patients within 3 years after surgical treatment. Metastasis is the major cause of death in these patients,\(^2,3,4\) and hepatic resection has been the only form of radical treatment in such cases. Although hepatic resection yields a favorable prognosis and better quality of life when compared with other forms of treatment, it is feasible in no >20% of patients.\(^5\) Therefore, it is important to identify alternative therapeutic methods to achieve disease control and radical cure. Minimally invasive approaches, such as radiofrequency thermal ablation (RFA), microwave thermal ablation (MWA), laser ablation, cryoablation, and high-intensity focused ultrasoundography,\(^6\) have been widely studied and have become the primary treatment option for patients with advanced disease wherein resection is impossible.

RFA and MWA are the 2 most common treatment options for CRLM. Previous retrospective studies have reported similar 5-year survival rates for both RFA and a single surgical procedure.\(^7,8,9\) Nonetheless, several studies have reported longer survival durations and fewer complications owing to RFA when compared with other regimens.\(^10,11,12\) The prognostic factors include the pretreatment carcinoembryonic antigen (CEA) level, tumor size, and tumor number, which can be used to predict recurrence and death following RFA.\(^13\)

Microwave coagulation was initially used for hemostasis or coagulation and was then gradually used as a definitive treatment modality for liver tumors.\(^14\) MWA was reported to be superior considering its larger ablation region, shorter operation time, and the ability to overcome the “heat sink” effect.\(^15,16\) Both MWA and RFA destroy the tumor via thermal energy and even entail a similar modality in that a probe is used to release energy in the center of the tumor. Several studies have shown that the factors related to the outcomes of MWA may also be applicable for RFA. Additionally, it is well established that RFA can improve survival outcomes in patients with liver metastasis.\(^12,17\) Unfortunately, only a few studies thus far have focused on the survival and treatment outcomes of MWA; moreover, prognostic factors for CRLM outcomes remain poorly understood.\(^18,19\) CEA has been the most commonly used biomarker for diagnosis and follow-up in colorectal cancer patients owing to its high accuracy and low cost. Some studies have shown that low CEA levels were positively correlated with longer progression-free survival (PFS) and overall survival (OS) in patients who underwent RFA.\(^19,20\) However, the prognostic value of CEA in patients who have undergone MWA remains unclear. Therefore, this study aimed to analyze the risk factors related to early recurrence in patients with CRLM treated with MWA.

2. Patients and methods

2.1. Patient population

Data for 140 consecutive patients who underwent MWA at our institution between January 2013 and December 2015 were retrospectively reviewed. Colorectal cancer patients with synchronous and metachronous liver metastases were included. The exclusion criteria were as follows (Fig. 1): underwent another ablation procedure before MWA (n = 10), tumors persisted after MWA (n = 3), presence of extrahepatic metastasis (including pulmonary, distant lymph nodes, and skeletal) (n = 24), and unrespectable primary tumor (n = 4). Owing to the retrospective nature of this study, written informed consent was obtained from all of the patients and the study was approved by the Clinical Research Ethics Committee of the Sixth Affiliated Hospital of Sun Yat-sen University.

All the patients were diagnosed with colorectal cancer via pathological examinations. Liver metastases were confirmed via adequate radiological imaging or biopsy before MWA. Patient demographics as well as laboratory data, imaging data, therapy protocol, and follow-up records were collected. Routine tests, such as complete blood counts, serum biochemical indices, and serum tumor markers were conducted within the week before MWA.

2.2. Treatment

The treatment strategies for individual patients with CRLM were discussed within a multi-disciplinary team (MDT) of experts including a colorectal surgeon, hepatobiliary specialist, diagnostic radiologist, interventional ultrasound physician, radiation oncologist, and medical oncologists.\(^21\) Subsequently, the treatment strategy would be explained to the patients and consent would be obtained.

In our institution, patients meeting the following criteria were selected to receive MWA: ineligibility for or failure of radical resection; tumor characteristics (presence of <5 tumors, tumor diameter of <5 cm, tumor location); and eligibility for MWA. Routine chemotherapy was performed according to the decision made by the MDT.
2.3. Microwave ablation

Informed consent was obtained from all patients prior to the MWA. Contrast-enhanced ultrasound (CEUS) was performed before MWA to confirm the size and the number of tumors, and after to eliminate hemorrhage, bile leakage, and incomplete ablation.

In our institution, MWA was performed using the KY2000 microwave treatment system (Nanjing KANYOU Medical Technology Co., Ltd.). For pain management during the percutaneous MWA, pethidine hydrochloride was administered intramuscularly (50–75 mg) approximately 30 minutes before the operation; moreover, local anesthesia was induced via topical injection of lidocaine (10–15 mL) at the beginning of the MWA. Patients underwent percutaneous MWA under real-time electrocardiographic monitoring and received low-flow oxygen.

Percutaneous MWA was performed under real-time ultrasound (LOGIQ E9, GE) guidance with a 1.0 to 5.0 MHz probe. Microwave radiation from the probe induces rapid oscillation in water molecules, causing frictional heating and consequent coagulation necrosis of the tissue surrounding the probe. The MWA was delivered at a frequency of 2450 MHz and a power of 30 to 100 W for 5 to 20 minutes using a 14-gauge (200 mm) cooled shift electrode (KY2450A, KANYOU Medical Technology Co., Ltd, Nanjing, China) (Fig. 2).

2.4. Follow-up

According to the protocols established at our institute, patients were followed every 3 months. Each visit includes a physical examination of the abdomen, serum CEA level, alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transpeptidase, bilirubin levels, and one or more imaging tests for the liver (CEUS, abdominal computed tomography, magnetic resonance imaging, and/or positron emission tomography–computed tomography) at the discretion of the MDT. Disease progression was defined as new tumors outside or inside the liver or local recurrence. PFS was calculated as the time from MWA to recurrence or death. However, liver progression-free survival (LPFS) was determined as the time from MWA to recurrence within the liver or death.

2.5. Statistical analysis

The patients were divided into a high and low CEA group on the basis of the median pretreatment CEA level. Mann–Whitney U tests were used to compare continuous variables at baseline according to their distributions, and the Pearson chi-square test was used to assess the categorical variables. Baseline characteristics including age, sex, tumor size, tumor number, presence of metastases, primary tumor node status, primary tumor location, and pre-MWA chemotherapy were compared between the 2 groups. The Kaplan–Meier method was used to analyze PFS, and the log-rank test was applied to compare the differences. A Cox proportional hazards model with backward stepwise selection was used to estimate the univariate and multivariate hazard ratio for the study variables. All the statistical analyses were performed using SPSS software (Version 22, IBM, INC, Armonk, New York, NY).

3. Results

3.1. Baseline characteristics

A total of 99 consecutive patients meeting the criteria were included in the current study. The median pretreatment CEA level was 3.7 (range: 0.63–514.41) ng/mL. The median PFS and LPFS duration following percutaneous MWA performed under ultrasound guidance were 9.0 (95% CI: 6.7–11.3) months and 11.5 (95% CI: 8.2–14.8), respectively. As shown in Table 1, there was no significant difference between the 2 groups regarding age, tumor number, primary tumor site, primary...
tumor node status, presence of metastases, and chemotherapy regimens. However, the high CEA group had a significantly higher number of male patients than the low CEA group (75.5% vs 56.0%, \( P = .040 \)). Unexpectedly, the number of patients with a tumor size >18 mm was significantly higher in the high CEA group than in the low CEA group (53.1% vs 24.0%, \( P = .003 \)). Moreover, the high CEA group had a significantly higher number of patients with a KRAS mutation (44.9% vs 16.0%, \( P = .003 \)).

The median follow-up period was 13 (range: 1–38) months. Overall, 66 (66.7%) patients had documented disease progression including local recurrence and extrahepatic progression following MWA; however, 58 (58.6%) patients were found to have hepatic progression, 3 (3.1%) patients died from tumor progression, and 13 (13.1%) patients were lost to follow up. The median PFS was 9 (95% confidence interval [CI]: 6.7–11.3) months for the whole cohort, 7.5 (95% CI: 2.2–12.8) months for the high CEA group, and 12.0 (95% CI: 7.3–16.7) months for the low CEA group.

### Table 1

| Variables                          | Overall (n=99) N (%) | Low CEA (n=50) N (%) | High CEA (n=49) N (%) | \( P \) value |
|------------------------------------|----------------------|----------------------|-----------------------|--------------|
| Age, y                             | .056                 |                      |                       |              |
| >55                                | 47 (47.5)            | 19 (38.0)            | 28 (57.1)             |              |
| ≤55                                | 52 (52.5)            | 31 (62.0)            | 21 (42.9)             |              |
| Lesion size, mm                    | .003                 |                      |                       |              |
| >18                                | 38 (38.4)            | 12 (24.0)            | 26 (53.1)             |              |
| ≤18                                | 61 (61.6)            | 38 (76.0)            | 23 (46.9)             |              |
| Gender                             | .040                 |                      |                       |              |
| Male                               | 65 (65.7)            | 28 (56.0)            | 37 (75.5)             |              |
| Female                             | 34 (34.3)            | 22 (44.0)            | 12 (24.5)             |              |
| Lesion number                      | .429                 |                      |                       |              |
| >3                                 | 21 (21.2)            | 9 (18.0)             | 12 (24.5)             |              |
| ≤3                                 | 78 (78.8)            | 41 (82.0)            | 37 (75.5)             |              |
| Primary site                       | .192                 |                      |                       |              |
| Right                              | 17 (17.1)            | 6 (12.0)             | 11 (22.4)             |              |
| Left                               | 82 (82.8)            | 44 (88.0)            | 36 (77.6)             |              |
| Regional lymphonodus status        | .317                 |                      |                       |              |
| Negative                           | 36 (36.4)            | 16 (32.0)            | 20 (40.8)             |              |
| Positive                           | 60 (60.6)            | 33 (66.0)            | 27 (55.1)             |              |
| Unknown                            | 3 (3.0)              | 1 (2.0)              | 2 (4.1)               |              |
| Metastases presentation            | .213                 |                      |                       |              |
| Synchronous                        | 69 (69.7)            | 32 (64.0)            | 37 (75.5)             |              |
| Metachronous                       | 30 (30.3)            | 18 (36.0)            | 12 (24.5)             |              |
| Preoperative chemotherapy          | 0.161                |                      |                       |              |
| No                                 | 48 (48.5)            | 28 (56.0)            | 20 (40.8)             |              |
| Yes                                | 51 (51.5)            | 22 (44.0)            | 29 (59.2)             |              |
| KRAS status                        | .003                 |                      |                       |              |
| Wild                               | 51 (51.5)            | 31 (62.0)            | 20 (40.8)             |              |
| Mutant                             | 30 (30.3)            | 8 (16.0)             | 22 (44.9)             |              |
| Unknown                            | 18 (18.2)            | 11 (22.0)            | 7 (14.3)              |              |
| Postoperative chemotherapy         | .952                 |                      |                       |              |
| No                                 | 26 (26.3)            | 13 (26.0)            | 13 (26.0)             |              |
| Yes                                | 73 (73.7)            | 37 (74.0)            | 36 (73.5)             |              |

All statistical tests were 2 sided. Statistical significance was defined as \( P < .05 \).

CEA = carcinoembryonic antigen.

3.2. Univariate and multivariate analysis of prognostic factors for PFS

Variables that might affect overall survival of patients with CRLM were subjected to univariable and multivariable Cox regression analysis. Patients with high CEA levels had a significantly lower 6-month PFS rate (54.7% vs 73.6%; \( P = .011 \)) than those with low CEA (hazard ratio [HR]: 1.85; 95% CI: 1.13–3.03; \( P = .014 \); Table 2, Fig. 3A). However, a similar association was not found for other tumor biomarkers including alpha-fetoprotein and carbohydrate antigen 19-9. The univariate analysis additionally indicated that male sex (\( P = .047 \)), >3 tumors (\( P = .002 \)), synchronous metastasis (\( P = .043 \)), and metastatic primary colorectal lymph nodes (\( P = .016 \)) were also significantly correlated with worse PFS (Table 2). Of note, age >55 years, tumor size >18 mm, and KRAS mutation were associated with the risk for disease progression, although without statistical significance, with an HR of 1.54 (95% CI: 0.94–2.50; \( P = .081 \)), 1.57 (95% CI: 0.96–2.50; \( P = .070 \)), and 1.735 (95% CI: 0.97–3.10; \( P = .063 \)), respectively.

Next, Cox multivariate analyses were applied to determine if the prognostic variables in the univariate analyses were independently related to PFS (Table 3). The results showed that high CEA level, >3 tumors, and positive node status for the primary tumor were independent factors for PFS, with corrected HRs of 2.11 (95% CI: 1.257–3.555; \( P = .005 \)), 2.450 (95% CI: 1.420–4.226; \( P = .001 \)), and 2.265 (95% CI: 1.304–3.935; \( P = .004 \)), respectively.

3.3. Univariate and multivariate analysis of prognostic factors for LPFS

In order to further explore the factors that predict LPFS, a survival analysis was also performed (Table 4). In patients with
CEA levels >3.7 ng/mL, the 6-month LPFS was 54.7%, versus 77.7% in patients with CEA levels ≤3.7 ng/mL (HR: 2.117; 95% CI: 1.247–3.593; P = .005; Table 2, Fig. 3B). A significant correlation was also noted for sex (HR: 1.825; 95% CI: 1.030–3.236; P = .039), tumor number (HR: 2.330; 95% CI: 1.332–4.077; P = .003), presence of metastases (HR: 2.234; 95% CI: 1.178–4.236; P = .014), and postoperative chemotherapy (HR: 0.505; 95% CI: 0.290–0.878; P = .016). However, factors such as age (P = .140), tumor size (P = .146), regional lymph node status (P = .072), and KRAS mutation (P = .122) were not associated with LPFS.

In the Cox multivariate analyses, a high CEA level was an independent prognostic factor for LPFS (HR: 2.333; 95% CI: 1.352–4.028; P = .002) (Table 5). The results showed that synchronous metastasis and >3 tumors were also independently associated with the risk for recurrence, with corrected HRs of 2.312 (95% CI: 1.149–4.632; P = .019) and 2.241 (95% CI: 1.231–4.077; P = .008), respectively and postoperative chemotherapy performed a protective role in recurrence, with corrected HRs of 0.306 (95% CI: 0.168–0.560; P < .001).

### Table 2

| Variables                        | PFS          | LPFS          |
|----------------------------------|--------------|---------------|
|                                 | 6-month rate (%) | Hazard ratio (95% CI) | P value | 6-month rate (%) | Hazard ratio (95% CI) | P value |
| Age, y                           | .081         | 1.541 (0.947–2.508) | .053 | 1.477 (0.879–2.482) | .140 |
| >55                              | 52.9         | 1              | 74.6 | 1              | .070         | 1              |
| ≤55                              | 54.9         | 1.576 (0.963–2.580) | 70.0 | 1              | .047         | 1              |
| Lesion size, mm                  | .070         | 1              | 72.3 | 1              | .002         | 1              |
| >18                              | 62.0         | 1.713 (1.008–2.910) | 69.2 | 1              | .002         | 1              |
| ≤18                              | 74.6         | 1              | 73.6 | 1              | .002         | 1              |
| Gender                           | .047         | 1              | 1    | 1              | .016         | 1              |
| Male                             | 60.4         | 1.893 (1.172–3.048) | 63.6 | 1.825 (1.030–3.236) | .039         | 1              |
| Female                           | 64.2         | 1              | 72.3 | 1              | .027         | 1              |
| Lesion number                    | .004         | 1              | 1    | 1              | .003         | 1              |
| >3                               | 58.8         | 1.070 (0.569–2.011) | 58.8 | 1.041 (0.487–1.819) | .057         | 1              |
| ≤3                               | 65.7         | 1              | 68.4 | 1              | .857         | 1              |
| Primary site                     | .833         | 1              | 1    | 1              | .857         | 1              |
| Right                            | 61.3         | 1.798 (1.018–3.179) | 62.8 | 2.234 (1.178–4.236) | .016         | 1              |
| Left                             | 71.8         | 1.070 (0.569–2.011) | 68.4 | 1              | .016         | 1              |
| Regional lymphonodus status      | .016         | 1              | 80.5 | 1              | .016         | 1              |
| Positive                         | 58.2         | 1.941 (1.130–3.335) | 58.2 | 1.677 (0.955–3.355) | .072         | 1              |
| Negative                         | 77.6         | 1              | 80.5 | 1              | .072         | 1              |
| Metastases presentation          | .043         | 1              | 1    | 1              | .043         | 1              |
| Synchronous                      | 61.3         | 1.798 (1.018–3.179) | 62.8 | 2.234 (1.178–4.236) | .016         | 1              |
| Metachronous                     | 71.8         | 1              | 75.4 | 1              | .946         | 1              |
| Preoperative chemotherapy        | .933         | 1              | 1    | 1              | .933         | 1              |
| No                               | 58.0         | 0.979 (0.603–1.590) | 64.2 | 0.946 (0.579–1.798) | .946         | 1              |
| Yes                              | 71.6         | 1              | 74.4 | 1              | .946         | 1              |
| CEA value, ng/mL                 | .014         | 1              | 1    | 1              | .014         | 1              |
| >3.7                             | 54.7         | 1.852 (1.131–3.034) | 54.7 | 2.117 (1.247–3.503) | .005         | 1              |
| ≤3.7                             | 73.6         | 1              | 77.7 | 1              | .005         | 1              |
| AFP value, ng/mL                 | .568         | 1              | 1    | 1              | .488         | 1              |
| >2.7                             | 68.8         | 1.152 (0.708–1.875) | 68.8 | 1.202 (0.714–2.023) | .488         | 1              |
| ≤2.7                             | 65.3         | 1              | 65.3 | 1              | .488         | 1              |
| CA199 value, U/mL                | .467         | 1              | 1    | 1              | .187         | 1              |
| >11.77                           | 57.1         | 1.197 (0.738–1.941) | 62.1 | 1.417 (0.844–2.379) | .187         | 1              |
| ≤11.77                           | 62.1         | 1              | 71.2 | 1              | .122         | 1              |
| KRAS status                      | .063         | 1              | 1    | 1              | .063         | 1              |
| Mutant                           | 49.3         | 1.735 (0.970–3.104) | 49.3 | 1.617 (0.879–2.977) | .122         | 1              |
| Wild                             | 72.4         | 1              | 74.4 | 1              | .122         | 1              |
| Postoperative chemotherapy       | .088         | 1              | 1    | 1              | .016         | 1              |
| Yes                              | 69.9         | 0.88 (0.367–1.071) | 72.2 | 0.505 (0.290–0.878) | .016         | 1              |
| No                               | 49.7         | 1              | 49.7 | 1              | .016         | 1              |

CEA = carcinoembryonic antigen, CI = confidence interval, LPFS = liver progression-free survival, PFS = progression-free survival.

Value are median.
4. Discussion

Patients with high pretreatment CEA level had a poorer PFS and LPFS outcome than those with low preoperative CEA levels. The prognostic value of CEA has been confirmed in patients with CRLM treated with RFA or hepatectomy. However, this study showed a direct correlation between CEA level and PFS or LPFS in CRLM patients treated with MWA.

The treatment outcomes of RFA have been widely investigated in several studies; however, only a few studies have focused on the long-term outcomes of MWA for CRLM. Compared with RFA, the potential benefits of MWA include a shorter ablation time, optimal heating of cystic masses, less procedural pain, and larger tumor ablation area. A prospective study showed that MWA produces a broader ablation region, overcomes the “heat sink” effect, and reduces skin burns.

Previous studies have reported that primary hepatocellular cancer patients treated with MWA had a long-term survival equivalent to that in patients treated with hepatectomy; moreover, MWA resulted in a lower local recurrence rate than that with RFA. Therefore, promising early outcomes after MWA, when compared with RFA, are expected. The median PFS duration in our cohort was 9 months, while the PFS duration after RFA in other cohorts ranged from 8 to 12 months. The disease progression rate and the liver progression rate in our study were 66.7% and 58.6%; however, previous studies have reported values of 60% to 77% and 43.3% and 62.3% with RFA, respectively. Iannitti et al. reported that the PFS rate at 19 months (median follow-up period) was 47%; the PFS rate was 33.3% in our series. However, these previous studies suggested a similar outcome: the high progression rate possibly results from both percutaneous ablation and CRLM.

In our study, the number of metastases, primary tumor nodal status, and CEA level were found to be independent prognostic factors for PFS. However, the independent prognostic factors for LPFS were sex, tumor number, and the CEA level. The CEA level was an independent prognostic factor for both PFS and LPFS. A similar outcome was also reported in a cohort of patients treated with hepatectomy, in which CEA level was the only tumor marker associated with the treatment outcomes.

Previous investigators have reported that CEA promotes cancer cell metastases and invasion by targeting the adherence junction complexes between cells and enhancing the aggregation of cancer cells. However, no significant difference was found in the tumor number according to CEA level in our study. CEA has also been demonstrated to play an important role in suppressing the immune system by inducing suppressor factor release from normal lymphocytes. These underlying biological mechanisms may explain why patients with high CEA levels had shorter PFS and LPFS.

Table 3

| Variables                      | Hazard ratio (95%CI) | P value |
|-------------------------------|----------------------|---------|
| More lesions                  | 2.450(1.420–4.226)   | .001    |
| Metastatic lymph nodes        | 2.265(1.304–3.935)   | .004    |
| High CEA value                | 2.114(1.257–3.555)   | .005    |

CEA = carcinoembryonic antigen, CI = confidence interval, PFS = progression-free survival.
LPFS. In the subgroup analysis, CEA level was also found to be an independent prognostic factor in men but not women. Therefore, the CEA level was a more reliable indicator in the male patients. The inconsistent value of some prognostic factors in different sexes has been demonstrated in patients with metastatic colorectal cancer, including epidermal growth factor receptor (EGFR) and methylenetetrahydrofolate reductase.\(^\text{[42,43]}\) The predictive role of CEA may be similar, but further studies are necessary to confirm this hypothesis.

The CEA level was also an independent prognostic factor in the subgroup with fewer tumors (≤5), in patients with a primary tumor node-positive status, and patients with primary tumors located in the right colon. The univariate analysis showed that primary tumor site was an insignificant factor in terms of LPFS. However, a significant difference was found in patients with tumors in the right colon. Although the number of the patients in this group was limited, colorectal patients with liver metastasis whose primary tumor site was the right colon may be at higher risk for recurrence. Previous studies have confirmed that right-sided colon cancers were more aggressive and associated with poorer clinical outcome.\(^\text{[44]}\)

Table 4

| Variables               | N (%)      | 6-month rate (high CEA group vs low CEA group%) | PFS         | Hazard ratio (95%CI) | P value   |
|-------------------------|------------|-----------------------------------------------|-------------|----------------------|-----------|
| Age                     |            |                                               |             |                      |           |
| >55                     | 47 (47.5)  | 45.5 vs 62.3                                 | 1.77 (0.853–3.671) | .125                 |
| ≤55                     | 52 (52.5)  | 60.0 vs 80.3                                 | 1.759 (0.884–3.501) | .108                 |
| Lesion size, mm         |            |                                               |             |                      |           |
| >18                     | 38 (38.4)  | 48.9 vs 66.7                                 | 1.678 (0.745–3.782) | .212                 |
| ≤18                     | 61 (61.6)  | 60.3 vs 75.9                                 | 1.715 (0.894–3.291) | .105                 |
| Gender                  |            |                                               |             |                      |           |
| Male                    | 65 (65.7)  | 52.2 vs 74.4                                 | 1.922 (1.028–3.933) | .041                 |
| Female                  | 34 (34.3)  | 61.1 vs 72.7                                 | 1.466 (0.606–3.549) | .396                 |
| Lesion number           |            |                                               |             |                      |           |
| >3                      | 21 (21.2)  | 35.7 vs 44.4                                 | 1.625 (0.635–4.158) | .311                 |
| ≤3                      | 78 (78.8)  | 60.1 vs 80.2                                 | 1.943 (1.081–3.493) | .026                 |
| Primary site            |            |                                               |             |                      |           |
| Right                   | 17 (17.2)  | 36.4 vs 83.3                                 | 6.005 (1.441–33.077) | .016                 |
| Left                    | 82 (82.8)  | 60.5 vs 70.0                                 | 1.468 (0.851–2.532) | .167                 |
| Regional lymphonodus status |          |                                               |             |                      |           |
| Negative                | 36 (36.4)  | 64.6 vs 93.8                                 | 2.275 (0.888–5.839) | .087                 |
| Positive                | 60 (60.6)  | 47.6 vs 66.0                                 | 2.034 (1.083–3.819) | .027                 |
| Metastases presentation |            |                                               |             |                      |           |
| Synchronous             | 69 (69.7)  | 55.1 vs 68.1                                 | 1.753 (0.972–3.160) | .062                 |
| Metachronous            | 30 (30.3)  | 52.1 vs 83.3                                 | 2.252 (0.741–6.025) | .106                 |
| KRAS status             |            |                                               |             |                      |           |
| Wild                    | 51 (51.5)  | 64.3 vs 77.4                                 | 1.465 (0.731–2.935) | .281                 |
| Mutant                  | 30 (30.3)  | 43.2 vs 62.5                                 | 2.962 (0.835–10.512) | .093                 |

CEA = carcinoembryonic antigen, CI = confidence interval, PFS = progression-free survival.

Table 5

| Variable                           | Hazard ratio (95%CI) | P value |
|------------------------------------|----------------------|---------|
| Synchronous metastasis             | 2.312 (1.149–4.652)  | .019    |
| More lesions                       | 2.241 (1.231–4.077)  | .008    |
| High CEA value                     | 2.333 (1.352–4.028)  | .002    |
| Postoperative chemotherapy          | 0.306 (0.168–0.560)  | <.001   |

CEA = carcinoembryonic antigen, CI = confidence interval, LPFS = liver progression-free survival.

There are several limitations in this study. Since the follow-up period was limited, only a few cases of death were recorded, and the OS data were not available for analysis. In addition, this study is also limited by its sample size and retrospective design. A further prospective study with a larger cohort and sufficient follow-up time will be necessary to validate our results and determine the predictive effect of CEA on OS.

In conclusion, our study showed that CRLM patients treated with MWA through CEUS had a median PFS duration of 9 months. Moreover, CEA could be a valuable prognostic factor for PFS in patients treated with MWA using CEUS with applications for treatment outcomes and following-up decisions.

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