A retrospective study comparing the efficacy of microwave ablation and stereotactic body radiotherapy in colorectal cancer lung metastases

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Abstract. The purpose of the present study was to assess and compare the efficacy of microwave ablation (MWA) and stereotactic body radiotherapy (SBRT) in the treatment of lung metastases from patients with colorectal cancer (CRC) and to identify the preferable treatment modality based on patient and tumor characteristics. Records of 118 patients with CRC with a total of 307 lung metastases who underwent SBRT or MWA between January 2015 and December 2022 were retrospectively analyzed, including the essential clinicopathological information on patients (age, sex and underlying diseases), diagnosis and treatment information [primary tumor site, levels of carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9], imaging data [diameter of lung metastasis, location of the metastasis (i.e., whether or not the tumor was adjacent to the vessel or bronchus) and internal features] and follow-up data (postoperative therapy, complications or adverse effects and survival outcomes). For statistical analysis of the local tumor progression (LTP), disease-free survival and overall survival (OS) rates, Cox regression analysis, along with the Kaplan-Meier method adjusted using inverse probability of treatment weighting (IPTW), were performed. The median follow-up duration in the present study was 31.5 months. Multivariable Cox regression analysis revealed that the CEA level, metastasis diameter and internal features were independent predictors of OS. In the IPTW-adjusted analysis, no significant difference in the 1-year OS rate was observed between the SBRT and MWA groups (92.9 vs. 93.9%; P=0.483); however, a notable discrepancy in the treatment modalities was noted, leading to significant differences in the 2- and 3-year OS rates (65.9 vs. 57.6%, P=0.001, and 44.7 vs. 36.4%, P<0.001, respectively). A significant interaction effect for the treatment modality was observed for LTP (P=0.021). In conclusion, the present study revealed that SBRT and MWA have similar therapeutic effects in terms of prolonging the survival of patients with CRC with lung metastases; however, regarding the local control of lung metastases, MWA is associated with a number of significant advantages.

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Abbreviations: MWA, microwave ablation; SBRT, stereotactic body radiotherapy; CRC, colorectal cancer; CEA, carcinoembryonic antigen; CA125, glycocalyx antigen 125; CA19-9, glycocalyx antigen 19-9; BMI, body mass index; IPTW, inverse probability of treatment weighting; LTP, local tumor progression; DFS, disease-free survival; OS, overall survival; RFA, radiofrequency ablation; LTPFS, local tumor progression-free survival; LTA, local tumor ablation; IQR, interquartile range; HR, hazard ratio; CI, confidence interval

Key words: microwave ablation, stereotactic body radiotherapy, colorectal cancer, lung metastases, prognosis

Introduction

Colorectal cancer (CRC) is one of the most common malignant tumors in the world, with its incidence steadily rising in developing countries. The mortality rate associated with CRC has risen to being the second highest worldwide, constituting ~10% of all fatalities attributed to malignant tumors (1). This is a widespread situation, given that 20-25% of patients present with distant metastases at the time of their initial diagnosis (2-4). The lung, ranked as the second most common site for CRC metastasis following the liver, poses a serious threat to patient survival (5,6). Surgery is considered the standard treatment for patients with resectable CRC lung metastases. In general, surgery is preferred for lung metastases from a single lesion with low morbidity and mortality when the patient is able to tolerate surgery and this treatment strategy has demonstrated 5-year survival rates of up to 70% (7). Surgery usually provides more complete treatment results and a means of more effective local control. However, surgery may be accompanied by a greater risk of trauma and postoperative complications

and therefore this treatment strategy requires that the patient be both in relatively good health and able to tolerate surgery. In clinical practice, only a minority of patients with CRC with lung metastases are eligible for surgical intervention. Numerous patients are unable to undergo surgery due to the presence of double lung metastases or multiple lesions, their having an advanced age, or because of comorbidities with unmanageable underlying diseases. Therefore, various nonsurgical approaches, including percutaneous ablation and stereotactic body radiotherapy (SBRT), are increasingly explored as alternative strategies for managing tumors in these patients.

Among the percutaneous ablation techniques, commonly employed methods include radiofrequency ablation (RFA), microwave ablation (MWA) and cryoablation. RFA is the most widely used and well-validated approach (8,9). MWA has also been demonstrated to be a safe and effective method for the treatment of CRC lung metastases, yielding a median overall survival (OS) of 31-32.8 months. Notably, it has exhibited distinct advantages in local tumor control compared with other ablation methods (10,11). Moreover, animal models have shown that MWA outperforms RFA in terms of ablation zone size and expansion of the ablation border, complete ablation and tumor control rates, sensitivity to the 'heat-sink effect' and reduced thermal conductivity of the ventilated lungs. These factors are crucial for sufficiently large lesions with a safe margin around the ablation zone (12-14). In addition, MWA boasts a shorter ablation time and a larger ablation range compared with RFA (14).

SBRT has emerged as a beneficial complement to non-surgical treatment methods for lung metastases, including those arising from CRC. SBRT can deliver high radiation doses to tumors while minimizing radiation exposure to the surrounding normal tissues, leading to a high rate of local tumor control and a tolerable level of toxicity as far as normal tissues are concerned. In comparison with surgery and ablative therapies, the key advantages of SBRT lie in its non-invasiveness, low morbidity, good tolerability and suitability for outpatient treatment (15). In terms of local control of CRC lung metastases, previously published studies on the efficacy of SBRT have shown considerable variability, with reported 2-year local control rates ranging from 65.8-80% (16-19). However, SBRT exhibits a distinct advantage over other methods for larger tumors near blood vessels and both the number and location of lung lesions and the presence of synchronous extrapulmonary metastases and mediastinal lymph metastases are important prognostic factors. Nevertheless, use of SBRT often leads to radiation pneumonitis during the treatment of lung metastases while the lesions shrink, causing irreversible damage to the lungs of patients (20).

MWA and SBRT have become standard non-surgical methods for lung metastases, demonstrating good efficacy in terms of local control of lung metastases as well as patient survival, similar to the level of efficacy observed with surgery (21). However, to date, to the best of our knowledge, there is still no universally recognized standard for selecting the most appropriate treatment approach. The literature supporting such a standard is also limited, leaving the choice between MWA and SBRT needing primarily to be made at the discretion of individual clinicians. In the context of lung metastases from CRC, there is currently a lack of studies that have directly compared the efficacies of MWA and SBRT. The objectives of the present study were therefore to compare the outcomes of MWA and SBRT for treating CRC lung metastases and try to contribute to the clarification of the selection standard.

Patients and methods

Patient population. Patients with CRC with lung metastases who were treated between January 2015 and December 2022 at Sir Run Run Shaw Hospital, Zhejiang University School of Medicine (Zhejiang, China) were included in the present study who met the following inclusion criteria: i) The patient was diagnosed with primary CRC based on pathological evidence; ii) clinical or pathological diagnosis of CRC lung metastases was made; iii) the first treatment the patient received was MWA or SBRT; and iv) complete clinical and imaging data were available. The exclusion criteria were as follows: i) The patient was aged <18 years; ii) poor image quality or significant artifacts were present; iii) the follow-up duration was <6 months; and iv) the metastases were combined with other primary tumors (Fig. 1). All procedures performed in the present study involving medical record information and data were approved by the Medical Ethics Committee of Sir Run Run Shaw Hospital (Zhejiang, China; project number 20230430).

MWA or SBRT treatments. The MWA procedures were performed by interventional radiologists with >8 years' experience in interventional oncology at the Sir Run Run Shaw Hospital. The ECO-100A1 microwave therapeutic instrument (ECO Medical Instrument Co., Ltd.), was used to perform MWA. The appropriate microwave ablation needle was selected according to the size and location of the tumor. Based on the location of the target tumor, patients were positioned accordingly (i.e., in the supine, lateral or prone position). The skin-to-tumor distance was measured on computed tomography (CT) images to determine the optimal puncture point and path for the ablation needle, guided by CT imaging. Accurate puncture of the lesion was performed under CT guidance and impedance monitoring and temperature control were employed to regulate the treatment process. Repeated CT scans were performed during ablation to confirm the coverage of the ablated area. If no apparent signs of bleeding were observed on the CT scans during the operation, the ablation needle was removed and the patient was sent back to the ward with local compression. In case of significant pneumothorax, thoracic puncture drainage was performed during the procedure.

For the SBRT procedure, patients were placed in the supine position to run chest CT localization scans. Radiation oncologists subsequently delineated the target area on the generated images. The gross target volume (GTV) was outlined on the CT lung window image, including the short burr roots around the lesion and the areas of pleural invasion. Lesions close to the mediastinum were carefully observed on mediastinal window images in order to assess their involvement in the mediastinum and surrounding tissues and the target area was modified accordingly. The planning target volume was generated by

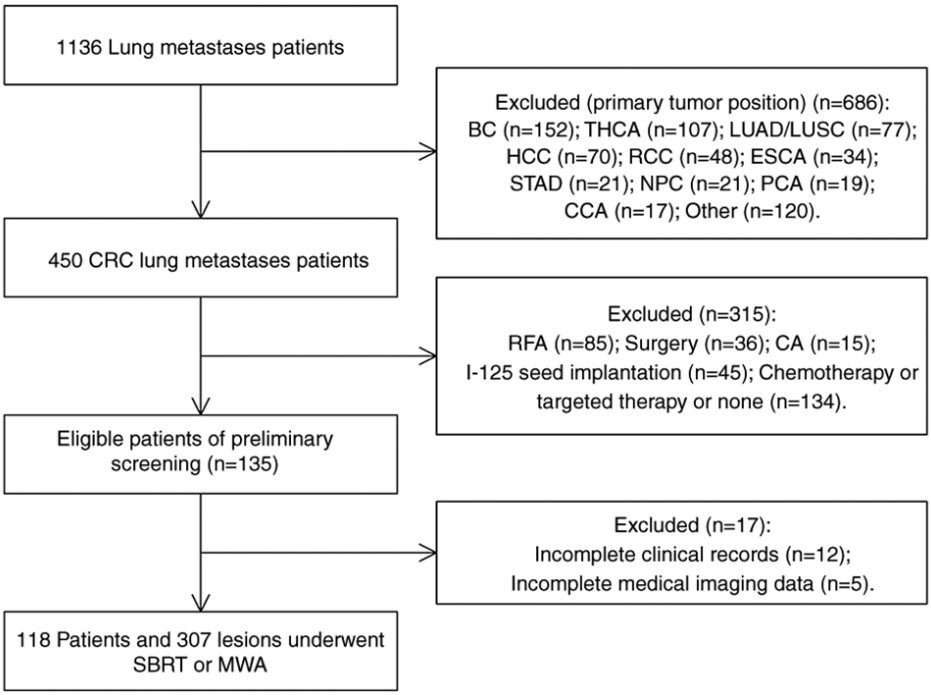

Figure 1. Flow diagram of patient selection. BC, breast cancer; THCA, thyroid carcinoma; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; HCC, hepatocellular carcinoma; RCC, renal cell carcinoma; ESCA, esophageal carcinoma; STAD, stomach adenocarcinoma; NPC, nasopharyngeal carcinoma; PCA, pancreatic cancer; CCA, cervical cancer; RFA, radiofrequency ablation; CA, cryoablation; SBRT, stereotactic body radiation therapy; MWA, microwave ablation.

expanding the GTV outlined on routine CT scans by 10 mm. The dose fractionation varied, with the majority of the treatments comprising five fractions or fewer and individual doses were typically of the order of 10 Gy, with adjustments made based on each patient's specific circumstances.

Follow-up and outcomes. All patients underwent follow-up using chest CT following treatment. After treatment, patients underwent chest CT scans monthly for the first three months, followed by scans every 2-3 months thereafter. The therapeutic outcomes between the MWA group and the SBRT group were compared by evaluating the LTP-free survival (LTPFS), disease-free survival (DFS) and OS rates. LTP was defined as either the recurrence of the treated tumor itself, or the emergence of a new local tumor within a 10-mm area around it on the CT images following treatment, whereas LTPFS was defined as the time interval from treatment to the occurrence of LTP, or to when the patient succumbed, or to loss to follow-up (22). DFS was defined as the duration from the initiation of MWA or SBRT to the detection of intra- or extra-pulmonary metastasis during follow-up examinations. Finally, OS values were calculated from the start of MWA or SBRT to either the death of the patient or the last follow-up date. Follow-up visits were conducted every three months, including recent patient visits to the hospital. If the patients had not visited the hospital recently, we called to inquire about their status, including survival and disease progression. During follow-up, the patients continued to receive treatments due to disease progression to prolong the survival including ablation, SBRT and chemotherapy. This was unavoidable in retrospective studies, although it affected the OS of patients.

Statistical analysis. In comparing patient characteristics between the SBRT and MWA groups, categorical variables were analyzed using the Chi-square (χ^2) test, whereas continuous variables that did not pass the K-S normality test were analyzed using the Mann-Whitney U-test. Univariate and multivariate analyses were performed using the Cox proportional hazards regression model to identify the potential factors affecting LTPFS, DFS and OS. To determine the prognostic factors, multivariate analysis using stepwise variable selection was performed. The Omnibus test was used to evaluate the COX regression model. To mitigate treatment selection bias and control for other potential confounding factors, inverse probability of treatment weighting (IPTW) was used for adjustment when comparing the OS, DFS and LTPFS between the MWA and SBRT groups, as well as the 1- and 3-year LTP, OS, DFS and LTPFS rates. For IPTW adjustments, patients in the MWA group were weighted as the inverse of the propensity score (PS), while patients in the SBRT group were weighted as the inverse of 1-PS. The PS was calculated as the probability of receiving MWA, determined through multivariate logistic regression analysis. The Hosmer-Lemeshow goodness-of-fit test was performed to evaluate the adequacy of the estimated PSs. Multivariate analysis included all covariates used to calculate the PS. All statistical analyses were conducted using SPSS v25 (IBM Corp.). $P<0.05$ was considered to indicate a statistically significant difference.

Results

Assessment of the patient characteristics. The present study screened 1,136 patients with lung metastases, of whom 450

were patients with CRC with lung metastases and 332 patients who did not meet the criteria were excluded (Fig. 1). A total of 118 patients were included in the present study, of which 85 (72.0%) patients with a total of 221 (out of an overall total of 307; 72.0%) lung metastases were treated with SBRT, whereas 33 (28.0%) patients with a total of 86 (out of an overall total of 307; 28.0%) lung metastases were treated with MWA. Seventy-three (65.3%) patients were male (see Table SI). Among the 118 patients, the body mass index (BMI) ranged from 17.3-31.2 kg/m^2 (mean, 23.67±3.04 kg/m^2. The primary site of the tumor was located in the rectum in a total of 76 (64.4%) cases. The degree of differentiation of the tumors was found to be predominantly moderately differentiated (n=56; 47.5%). Neoadjuvant therapy at the primary site was performed in 45 (38.1%) patients. A total of 48 patients (40.7%) were found to have solitary lung metastases. The liver was the most common extrapulmonary organ. The essential characteristics of the lung metastases are shown in Table SII. The mean size of the metastatic lesions was 11.80±8.13 mm. Finally, 53 (17.3%) of the lesions exhibited internal features. The internal features in this manuscript refer to cavity, vacuole sign or air bronchogram sign. During follow-up, 63 patients in the SBRT group received postoperative chemotherapy and 53 patients received targeted therapy; seven patients received particle therapy because of progression and four patients received ablative therapy. A total of 22 patients in the MWA group received postoperative chemotherapy and 19 patients received targeted therapy; one patient received particle therapy because of progression and four patients received ablative therapy.

Characteristics of the patients and their lesions are shown in Table I. Statistically significant differences were observed between the SBRT and MWA groups regarding the diameter of the metastasis, preoperative targeted therapy, concurrent extrapulmonary metastasis, proximity to the diaphragm, pneumothorax, local progression and postoperative adjuvant treatment (P<0.05). Subsequently, the effects of different treatment modalities on the OS, DFS and LTPFS rates were further analyzed. The Kaplan-Meier method was used to reveal that the MWA group did not reach the median survival time. Furthermore, the differences in DFS and LTPFS between the two treatment groups were found to be statistically significant (P=0.022), although no significant difference was observed in terms of the OS (P=0.064).

Analysis of LTP values. The median follow-up duration for the SBRT group was found to be 32 months [interquartile range (IQR), 20-44 months], whereas for the MWA group, it was 26 months (IQR, 17-47 months). Throughout the follow-up period, local progression was observed in 121 of the 307 lesions (39.4%). Specifically, 96 out of 221 (43.4%) lesions in the SBRT group and 25 out of 86 (29.1%) lesions in the MWA group exhibited local progression. The difference in 1-year LTP between the SBRT and MWA groups was found to be insignificant (29.0 vs. 19.8%; P=0.101), although a significant difference was observed for the 3-year LTP (43.0 vs. 29.1%; P=0.025) (Table II). However, following IPTW adjustment, significant differences in the 1-year and 3-year LTP rates were observed between the two groups (P<0.001).

The data from the univariate and multivariate analyses for the predictors of LTPFS are summarized in Table III. According to the univariate analysis, the potential predictors for LTPFS included extrapulmonary metastases [hazard ratio (HR), 1.884; 95% confidence intervals (95% CI), 1.066-3.327; P=0.029)], the level of carbohydrate antigen 19-9 (CA19-9; HR, 2.204; 95% CI, 1.109-4.382; P=0.024), metastasis diameter (HR, 1.564; 95% CI, 1.121-2.181; P=0.009), internal features (HR, 1.760; 95% CI, 1.180-2.624; P=0.006), local progression (HR, 3.649; 95% CI, 2.524-5.274; P<0.001) and treatment modality (HR, 0.431; 95% CI, 0.203-0.913; P=0.028). Subsequently, the multivariate analysis showed that the CA199 level (HR, 2.487; 95% CI, 1.263-4.901; P=0.008), metastasis diameter (HR, 1.485; 95% CI, 1.060-2.080; P=0.021), internal features (HR, 1.642; 95% CI, 1.097-2.459; P=0.016), local progression (HR, 3.649; 95% CI, 2.524-5.274; P<0.001) and treatment modality (HR, 0.408; 95% CI, 0.192-0.867; P=0.020) were significant predictors of LTPFS. In both the univariate and IPTW-adjusted analyses, LTPFS was found to significantly differ between the SBRT and MWA groups (Table IV). However, no significant differences in the 1-year and 3-year LTPFS rates were observed between the two groups with or without IPTW adjustment (67.1 vs. 69.7%; P=0.077; and 14.1 vs. 18.2%, P=0.204 for 1- and 3-year LTPFS, respectively; Table II). Subsequently, the associations of metastasis diameter, local progression and treatment modality were further explored, between the two treatment groups. The results obtained showed that no significant difference in the association of lesion diameter with local progression was observed (P=0.099), although the difference between local progression and treatment modality was significant (P=0.021). Stratifying the metastasis diameter to explore the local control effect between the two groups revealed that the difference between the two treatment modalities with metastasis diameter >20 mm (71.4 vs. 51.9%; P=0.426) was insignificant (Table V). Moreover, when the metastasis diameter was ≤20 mm, no statistically significant difference between the two groups in terms of the metastasis diameter was noted (P=0.248), although MWA was superior to SBRT in terms of local control (70.9 vs. 57.2%; P=0.037). Similarly, when the metastasis diameter was ≤10 mm, no statistically significant difference was observed in the metastasis diameter between the two groups (P=0.528), although MWA was again superior to SBRT in terms of local control (76.3 vs. 57.1%; P=0.016). Therefore, the effect of the metastasis diameter on local control in the two groups could be discounted (i.e. no significant difference was found between the metastasis diameter and local control). It could also be confirmed that MWA was superior to SBRT in terms of local control.

Analysis of OS rates. Data from the univariate and multivariate analyses for the predictors of OS are summarized in Table VI. In the univariate analysis, the potential predictors for OS included extrapulmonary metastases (HR, 1.850; 95% CI, 1.036-3.303; P=0.038), the carcinoembryonic antigen (CEA) level (HR, 2.089; 95% CI, 1.212-3.598; P=0.008), metastasis diameter >10 mm (HR, 1.600; 95% CI, 1.149-2.228; P=0.005), internal features (HR, 1.618; 95% CI, 1.089-2.402; P=0.017) and treatment modality (HR, 0.501; 95% CI, 0.236-1.062; P=0.071). After having incorporated the aforementioned variables into the multivariate Cox regression model, the results obtained showed that the CEA level (HR, 2.089; 95% CI, 1.212-3.598; P=0.008), metastasis diameter (HR, 1.534; 95%

Table I. Patient characteristics.

Variable	SBRT (n=85)	MWA (n=33)	P-value
Age (mean, IQR)	61 (55-66)	58 (55-67)	0.824
≤70 years (%)	71 (83.5)	27 (81.8)	
>70 years, n (%)	14 (16.5)	6 (18.2)	
Sex, male (%)	54 (63.5)	23 (69.7)	0.528
Primary cancer location (rectum)	54 (63.5)	23 (69.7)	0.528
Lung lobe distribution			0.169
Left, n (%)	17 (20.0)	10 (30.3)	
Right, n (%)	32 (37.6)	15 (45.5)	
Both, n (%)	36 (42.4)	8 (24.2)	
Neoadjuvant therapy, n (%)	35 (41.2)	10 (30.3)	0.275
Preoperative targeted therapy, n (%)	10 (11.8)	9 (27.3)	0.040[a]
Extrapulmonary metastases, n (%)	57 (67.1)	13 (39.4)	0.006[a]
Underlying diseases, n (%)	47 (55.3)	16 (48.5)	0.506
BMI (<18.5 or >23.9 kg/m^2), n (%)	40 (47.1)	17 (51.2)	0.664
CEA (>5.0 ng/ml), n (%)	30 (35.3)	11 (33.3)	0.841
Preoperative emphysema (%)	17 (20.0)	5 (15.2)	0.544
Preoperative lung bullae, n (%)	10 (11.8)	7 (21.2)	0.308
Hilar lymphadenopathy, n (%)	2 (2.4)	1 (3.0)	1.000
Mediastinal lymphadenopathy, n (%)	3 (3.5)	1 (3.0)	1.000
Pneumothorax			<0.001[a]
None, n (%)	85 (100)	11 (33.3)	
Little, n (%)	0 (0.0)	14 (42.4)	
Moderate to large, n (%)	0 (0.0)	8 (24.2)	
Adjuvant (postoperative) therapy, n (%)	69(81.2)	24 (72.7)	0.014[a]
Metastasis diameter, mm. mean	12.553±8.545	9.871±6.624	0.001[a]
Adjacent to vessels >3 mm, n (%)	37 (16.7)	11 (12.8)	0.392
Adjacent to vessels >5 mm, n (%)	18 (8.1)	5 (5.8)	0.486
Adjacent to the bronchus >2 mm, n (%)	39 (17.6)	20 (23.2)	0.263
Near mediastinal pleura 10 mm, n (%)	33 (14.9)	10 (11.6)	0.454
Near chest wall pleura 10 mm, n (%)	90 (40.7)	31 (36.0)	0.451
Near pleura 0.5 mm, n (%)	53 (24.0)	13 (15.1)	0.090
Near interlobar pleura 10 mm, n (%)	49 (22.2)	17 (19.8)	0.645
Near the diaphragm 10 mm, n (%)	28 (12.7)	4 (4.7)	0.039[a]
Internal features, n (%)	38 (17.2)	15 (17.4)	0.959
Local progression, n (%)	96 (43.4)	25 (29.1)	0.021[a]

The internal features refer to cavity, vacuole sign or air bronchogram sign. [a]P<0.05. SBRT, stereotactic body radiotherapy; MWA, microwave ablation; IQR, interquartile range; BMI, body mass index; CEA, carcinoembryonic antigen.

CI, 1.098-2.143; P=0.012) and internal features (HR, 1.608; 95% CI, 1.078-2.400; P=0.020) served as independent predictors of OS. The Omnibus test for model coefficients indicated that there was a statistically significant difference (χ^2=7.355, P=0.007). The 1-year and 3-year rates of OS were respectively found to be 92.9 and 44.7% in the SBRT group and 93.9 and 36.4% in the MWA group (IPTW-adjusted: 1-year: P=0.354; 3-year: P<0.001; Table II). According to the univariate analysis, the difference in OS between the SBRT and MWA groups was not significantly significant (P=0.071), although, after IPTW adjustment, a substantially significant difference was noted between the two groups (P<0.001; Table IV).

Kaplan-Meier method was subsequently used to analyze the variables that showed significant differences according to the multivariate Cox regression models. Although no significant differences in treatment modality were noted for the OS values, the OS data were still included in the study after IPTW adjustment, since the P-value was <0.05. The results obtained showed that patients with regular CEA levels had a median OS of 57 months (95% CI, 43.997-70.003), which was higher compared with that in patients who had an abnormal CEA level (26 months; 95% CI, 16.482-35.518; P=0.006; Fig. 2A). For CRC patients with lung metastases with a metastasis diameter >10 mm, the median OS was 36 months (95% CI,

Table II. Comparison of 1- and 3-year LTP, OS, DFS and LTPFS for MWA and SBRT.

Variable	SBRT (%)	MWA (%)	P-value (before)	P-value (IPTW-adjusted)
LTP				
1-year	64 (29.0)	17 (19.8)	0.101	<0.001[a]
3-year	95 (43.0)	25 (29.1)	0.025[a]	<0.001[a]
OS				
1-year	79 (92.9)	31 (93.9)	1.000	0.354
3-year	38 (44.7)	12 (36.4)	0.410	<0.001[a]
DFS				
1-year	38 (44.7)	17 (51.5)	0.506	<0.001[a]
3-year	6 (7.1)	4 (12.1)	0.604	0.016[a]
LTPFS				
1-year	57 (67.1)	23 (69.7)	0.783	0.077
3-year	12 (14.1)	6 (18.2)	0.582	0.204

[a]P<0.05. LTP, local tumor progression; OS, overall survival; DFS, disease-free survival; LTPFS, local tumor progression-free survival; SBRT, stereotactic body radiotherapy; MWA, microwave ablation.

29.422-42.578), which was a shorter time compared with that in patients with lung metastases with a metastasis diameter ≤10 mm (57 months; 95% CI, 51.757-62.243; P=0.004; Fig. 2B). The median OS was determined to be 36 months for patients with internal features (95% CI, 35.492-44.508), which was shorter than that for patients with solid tumors (48 months; 95% CI, 41.100-54.900; P=0.014; Fig. 2C). The median OS for patients in the SBRT group was 40 months; by contrast, for the MWA group, the median observation duration was not reached. Ultimately, for the two treatment modalities, the difference in OS was not found to be statistically significant (χ^2=3.442, P=0.064; Fig. 2D).

Analysis of the DFS rates. During the follow-up period, tumor recurrence occurred in 73 patients in the SBRT group (intrapulmonary recurrence, n=55; extrapulmonary recurrence, n=18) and 27 patients in the MWA group (intrapulmonary recurrence, n=18; extrapulmonary recurrence, n=9). The 1-year and 3-year DFS rates were found to be 44.7 and 7.1% in the SBRT group and 51.5 and 12.1% in the MWA group, respectively (IPTW-adjusted: 1-year: P<0.001; 3-year: P=0.016; Table II). DFS refers to more than local progression, but also includes recurrence of the primary focus and distant metastases. LTPFS is more indicative of local control than DFS. Data from the univariate and multivariate analyses of the predictors of DFS are summarized in Table VII. The univariate analysis revealed that extrapulmonary metastases (HR, 1.967; 95% CI, 1.112-3.481; P=0.020), the CEA level (HR, 1.725; 95% CI, 1.003-2.964; P=0.049), internal features (HR, 1.511; 95% CI, 1.018-2.242; P=0.040), local progression (HR, 2.041; 95% CI, 1.449-2.875; P<0.001) and the treatment modality (HR, 0.432; 95% CI, 0.204-0.916; P=0.029) were potential predictors of DFS and the differences were shown to be statistically significant (P<0.05). Incorporating the aforementioned variables into the multivariate Cox regression model, the results showed that internal features (HR, 1.511; 95% CI, 1.018-2.242; P=0.040), local progression (HR, 2.041; 95% CI, 1.449-2.875; P<0.001) and the treatment modality (HR, 0.413; 95% CI, 0.195-0.876; P=0.021) were independent predictors of DFS. According to both the univariate and IPTW-adjusted analyses, significant differences in DFS were observed between the SBRT and MWA groups (Table IV).

The Kaplan-Meier method was subsequently applied for variables that showed significant differences according to the multivariate Cox regression models. The results showed that the median DFS for patients in the SBRT group was 18 months (95% CI, 10.611-25.389), whereas for the MWA group, the median observation duration was not reached. A statistically significant difference in the DFS values was identified between the two treatment modalities (χ^2=5.226, P=0.022; Fig. 3A). The median DFS was 12 months for patients with internal features (95% CI, 3.778-20.222), which was shorter compared with the median DFS for patients with solid tumors (23 months; 95% CI, 18.960-27.040; χ^2=4.492; P=0.034; Fig. 3B). The median DFS for patients with local progression of lung metastases was determined to be 11 months (95% CI, 7.902-14.098), which was shorter than that for patients who experienced no local progression of lung metastases (25 months; 95% CI, 22.274-27.726; χ^2=18.220; P<0.001; Fig. 3C).

Analysis of treatment complications. MWA and SBRT, as treatment modalities, were both found to be well tolerated and no patients succumbed to treatment-associated mortality. In the MWA group, pneumothorax complications occurred in 22 (66.7%) patients, with eight (24.2%) of the patients experiencing a moderate-to-large pneumothorax that required thoracocentesis drainage (although this process resulted in the issue being resolved satisfactorily for the majority of the patients within a week). In addition, 14 patients (42.4%) developed pleural effusions, although only one patient developed massive pleural effusions. In the SBRT group, 54 (63.5%) of the patients developed radiation pneumonitis within 1-3 months following treatment, with 29 (34.1%) of the patients showing signs of inflammation at ~3 months post-irradiation.

Table III. Uni- and multivariate analyses for local tumor progression-free survival.

	Univariate analysis		Multivariate analysis	
Variable	HR (95% CI)	P-value	HR (95% CI)	P-value
Age, ≥70 years	1.178 (0.593-2.339)	0.639		
Sex, female	0.771 (0.440-1.350)	0.362		
BMI, <18.5 or >23.9 kg/m^2	0.709 (0.415-1.211)	0.209		
Primary cancer location, colon	0.956 (0.532-1.716)	0.880		
Extrapulmonary metastases	1.884 (1.066-3.327)	0.029[a]		
Underlying diseases	1.204 (0.701-2.069)	0.502		
Preoperative emphysema	0.967 (0.499-1.874)	0.920		
Preoperative lung bullae	1.450 (0.647-3.250)	0.367		
Hilar lymphadenopathy	1.132 (0.274-4.669)	0.864		
Mediastinal lymphadenopathy	1.829 (0.440-7.600)	0.406		
Lung lobe distribution				
Right	0.565 (0.287-1.110)	0.098		
Both	0.976 (0.499-1.911)	0.945		
CEA, ≥5.0 ng/ml	1.630 (0.951-2.791)	0.075		
CA19-9, ≥37.0 IU/ml	2.204 (1.109-4.382)	0.024[a]	2.487 (1.263-4.901)	0.008[a]
CA125, ≥35.0 U/ml	1.426 (0.440-4.623)	0.544		
Treatment modality, MWA	0.431 (0.203-0.913)	0.028[a]	0.408 (0.192-0.867)	0.020[a]
Neoadjuvant therapy	0.863 (0.499-1.491)	0.597		
Preoperative targeted therapy	0.736 (0.332-1.631)	0.450		
Preoperative I-125 seed implantation	0.530 (0.129-2.182)	0.379		
Metastasis diameter >10 mm	1.564 (1.121-2.181)	0.009[a]	1.485 (1.060-2.080)	0.021[a]
Adjacent to vessels >3 mm	1.250 (0.783-1.994)	0.350		
Adjacent to vessels >5 mm	1.029 (0.541-1.958)	0.931		
Adjacent to the bronchus >2 mm	1.112 (0.715-1.730)	0.638		
Near mediastinal pleura 10 mm	1.215 (0.756-1.953)	0.422		
Near chest wall pleura 10 mm	1.228 (0.881-1.711)	0.225		
Near pleura 0.5 mm	1.165 (0.772-1.758)	0.467		
Near interlobar pleura 10 mm	0.919 (0.627-1.347)	0.666		
Near the diaphragm 10 mm	1.028 (0.611-1.732)	0.916		
Internal features	1.760 (1.180-2.624)	0.006[a]	1.642 (1.097-2.459)	0.016[a]
Local progression	3.649 (2.524-5.274)	<0.001[a]	3.649 (2.524-5.274)	<0.001[a]
Adjuvant (postoperative) therapy	1.564 (0.784-3.120)	0.205		

[a]P<0.05. HR, hazard ratio; CI, confidence interval; BMI, body mass index; CEA, carcinoembryonic antigen; CA19-9, glycocalyx antigen 19-9; CA125, glycocalyx antigen 125; SBRT, stereotactic body radiotherapy.

Discussion

For patients with CRC with lung metastases, in addition to the traditional treatment of surgical resection, emerging treatments, including percutaneous ablation therapy and SBRT, have gradually attracted attention in recent years. The most commonly used percutaneous ablation therapy is RFA; moreover, in recent years, the application of MWA in the treatment of metastases that are difficult to resect by surgery has also gradually increased. In the present study, the MWA group had a total of 21 lung metastases with LTP; their maximum diameters ranged from 3.5-24.7 mm (median diameter: 10.1 mm). LTP was found not to exert any significant impact on OS (P=0.842) and this finding was consistent with the findings of the study published by Kurilova *et al* (23).

Cheng *et al* (10) reported that 32 patients with CRC with 48 lung metastases were treated with MWA and the 1-, 2- and 3-year OS rates were found to be 79.5, 63.1 and 44.4%, respectively. In a study by Yang *et al* (24) on the treatment of non-small cell lung cancer using MWA, the 1-, 2- and 3-year OS rates were reported to be 89, 63 and 43%, respectively. In the present study, the 1-, 2- and 3-year OS rates following MWA treatment were found to be 93.9, 57.6 and 36.4%, respectively, which were similar to those reported in the aforementioned studies.

Delpla *et al* (25) discussed the role of thermal ablation in the treatment of CRC lung metastases and presented the main results based on 12 relevant studies. They found that the incidence of local control ranged from 62-91%, which broadly

Table IV. HR for oncological outcomes according to treatment modality.

Outcome	Method	HR (95% CI)	P-value
Overall survival	Univariate	0.501 (0.236-1.062)	0.071
	IPTW-adjusted	0.559 (0.464-0.674)	<0.001[a]
Disease-free survival	Univariate	0.432 (0.204-0.916)	0.029[a]
	IPTW-adjusted	0.495 (0.411-0.597)	<0.001[a]
Local tumor progression-free survival	Univariate	0.431 (0.203-0.913)	0.028[a]
	IPTW-adjusted	0.485 (0.441-0.533)	<0.001[a]

[a]P<0.05. HR, hazard ratio; CI, confidence interval; IPTW, inverse probability of treatment weighting.

Table V. Stratified exploration of the comparison between the two groups in terms of metastasis diameter and local control.

Variable	SBRT	MWA	P-value
Metastasis diameter >20 mm			
Mean, mm)	30.759	27.971	0.456
Local control	14 (51.9%)	5 (71.4%)	0.426
Metastasis diameter ≤20 mm			
Mean, mm)	10.019	8.267	0.248
Local control	111 (57.2%)	56 (70.9%)	0.037[a]
Metastasis diameter ≤10 mm			
Mean, mm)	6.962	6.764	0.528
Local control	60 (57.1%)	45 (76.3%)	0.016[a]

[a]P<0.05. SBRT, stereotactic body radiotherapy; MWA, microwave ablation.

aligns with the results of the MWA group in the present study (70.9%). Local control has improved in recent studies, possibly due to technological advances and patient/tumor selection and this has been accomplished through an improved knowledge of the risk factors for local recurrence of tumors.

In the present study, the multivariate analysis showed that metastasis diameter was a prognostic factor for both OS and DFS and these findings were consistent with those of previous studies (26-28). It has been reported that independent predictors of OS also include the location of the primary disease (26), tumor stage (27), the number of metastases (26), metastasis diameter (26-28) and extrapulmonary metastases (29). The findings of the present study supported that extrapulmonary metastases is a potential predictor of OS (P=0.038), but significant differences were not revealed according to the multivariate analysis. Additionally, it found that internal features of lung metastases significantly differed in terms of the OS, LTPFS and DFS values (P<0.05), demonstrating that these could also serve as prognostic factors for survival.

CEA, CA19-9 and CA125 were selected for this present study. CEA is a serum glycoprotein and currently is the most widely used marker for colon cancer (30). CA19-9 is an antigen that elevated in numerous types of gastrointestinal cancer including colorectal cancer, esophageal cancer and hepatocellular carcinoma (31). CA125 is a glycoprotein antigen that is associated with gastric, colon, lung, pancreatic and liver cancers, as well as types of blood cancer (32). The present study found that CEA was a prognostic factor for OS and CA19-9 was an independent predictor of LTPFS. In colorectal cancers, other markers such as CA50, CA724 are also suitable markers. CA50 is an independent prognostic factor for patients with CRC following radical resection and CA724 is a glycoprotein, with higher levels in colorectal cancer (33). CSLEX and NCC-ST-439 are tumor-associated carbohydrate antigens that can identify colon cancer (34). The combination assay of serum CEA, CA 19-9, STn and SLX will be beneficial for diagnosis and follow-up of colorectal cancer (35). Unfortunately, the data for these markers are poor and that is one of the limitations of the present study.

The results of the present study emphasized the potential of using MWA, especially for the treatment of surgically unresectable CRC lung metastases. However, clinicians still need to carefully select the most appropriate treatment modality and to consider the characteristics of the lesion, the patient's overall condition and the long-term outcome of the treatment in patient-individualized treatment decisions.

On the other hand, in addition to thermal ablation techniques, SBRT has attracted much attention as a useful addition to the treatment of CRC lung metastases. Sharma *et al* (36) reported on 118 patients with CRC with a total of 202 lung metastases who were treated with SBRT and the 2-, 3- and 5-year OS rates were reported to be 69, 55 and 36%,

Table VI. Univariate and multivariate analyses for overall survival.

	Univariate analysis		Multivariate analysis	
Variable	HR (95% CI)	P-value	HR (95% CI)	P-value
Age, >70 years	1.094 (0.550-2.175)	0.797		
Sex, female	0.809 (0.463-1.416)	0.459		
BMI, <18.5 or >23.9 kg/m^2	0.797 (0.466-1.364)	0.409		
Primary cancer location, colon	0.769 (0.429-1.381)	0.380		
Extrapulmonary metastases	1.850 (1.036-3.303)	0.038[a]		
Underlying diseases	1.203 (0.703-2.061)	0.500		
Preoperative emphysema	0.807 (0.405-1.605)	0.541		
Preoperative lung bullae	0.958 (0.433-2.124)	0.917		
Hilar lymphadenopathy	0.395 (0.054-2.891)	0.361		
Mediastinal lymphadenopathy	0.609 (0.084-4.425)	0.624		
Lung lobe distribution				
Right	0.622 (0.315-1.226)	0.170		
Both	0.741 (0.379-1.449)	0.380		
CEA, ≥5.0 ng/ml	2.089 (1.212-3.598)	0.008[a]	2.089 (1.212-3.598)	0.008[a]
CA19-9, ≥37.0 IU/ml	1.745 (0.880-3.459)	0.111		
CA125, ≥35.0 U/ml	1.833 (0.364-9.216)	0.430		
Treatment modality, MWA	0.501 (0.236-1.062)	0.071		
Neoadjuvant therapy	1.050 (0.610-1.808)	0.860		
Preoperative targeted therapy	1.043 (0.470-2.313)	0.918		
Preoperative I-125 seed implantation	0.650 (0.158-2.675)	0.551		
Metastasis diameter ≥10 mm	1.600 (1.149-2.228)	0.005[a]	1.534 (1.098-2.143)	0.012[a]
Adjacent to vessels over 3 mm	1.317 (0.825-2.102)	0.249		
Adjacent to vessels over 5 mm	0.973 (0.510-1.857)	0.933		
Adjacent to the bronchus over 2 mm	1.136 (0.731-1.766)	0.570		
Near mediastinal pleura 10 mm	0.884 (0.551-1.419)	0.610		
Near chest wall pleura 10 mm	1.066 (0.764-1.488)	0.705		
Near pleura 0.5 mm	0.951 (0.632-1.430)	0.808		
Near interlobar pleura 10 mm	1.202 (0.820-1.763)	0.345		
Near the diaphragm 10 mm	1.028 (0.611-1.732)	0.916		
Internal features	1.618 (1.089-2.402)	0.017[a]	1.608 (1.078-2.400)	0.020[a]
Local progression	1.035 (0.741-1.444)	0.842		
Adjuvant postoperative therapy	1.413 (0.690-2.895)	0.344		

[a]P<0.05. HR, hazard ratio; CI, confidence interval; BMI, body mass index; CEA, carcinoembryonic antigen; CA125, glycocalyx antigen 125; CA19-9, glycocalyx antigen 19-9; SBRT, stereotactic body radiotherapy.

respectively. In the present study, the 2- and 3-year OS rates following SBRT treatment were found to be 65.9 and 44.7% respectively, which were a little lower than those reported in their study. It was not possible to calculate the 5-year survival period in Sharma *et al* (36), since the follow-up duration was relatively short and there were few patients with a survival period exceeding 5 years. In their meta-analysis, Zhang *et al* (37), found that having a single metastasis was a protective factor for OS, which aligned with the results of the present study.

To the best of the authors' knowledge, no studies have been published which have directly compared the treatment methods of SBRT and MWA in patients with CRC with lung metastases. Therefore, the present study may represent the first retrospective analysis that has been focused on this particular topic. In the present study, 118 patients with CRC who had a total of 307 lung metastases underwent SBRT or MWA treatment. Multivariate COX regression analysis revealed that the level of CA199, metastasis diameter, internal features and the treatment modality were significant predictors of LTPFS. Among these factors, lung metastases with a normal level of CA199, metastases of diameter ≤10 mm, tumors without internal features and those treated with MWA achieved improved local tumor control.

Ager *et al* (38) demonstrated the superiority of SBRT over percutaneous local tumor ablation in terms of the OS rate in their study on early-stage non-small cell lung cancer (1-year OS: 87.5 vs. 83.5%; 2-year OS: 68.0 vs. 63.0%; 3-year OS: 52.5

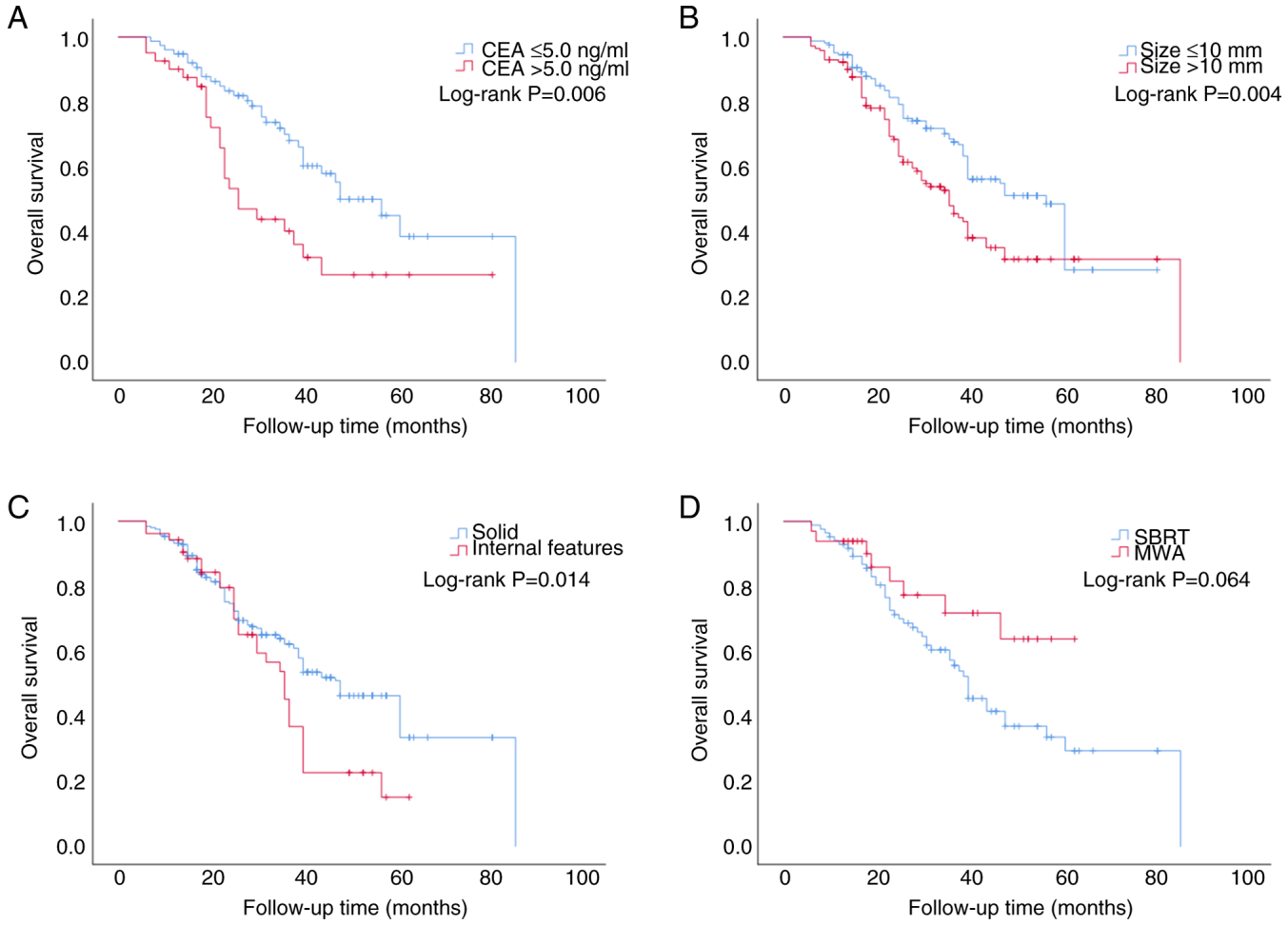

Figure 2. Kaplan-Meier method for overall survival. The effects of (A) CEA level, (B) metastasis diameter, (C) internal features of lung metastases and (D) the treatment modality on OS. CEA, carcinoembryonic antigen; OS, overall survival; SBRT, stereotactic body radiation therapy; MWA, microwave ablation.

vs. 45.9%; P<0.001). The results of the present study indicated that, following IPTW adjustment, no significant differences were observed in the 1-year OS rates regarding the lung metastases of patients with CRC having been treated with SBRT or MWA (92.9 vs. 93.9%, P=0.354). However, differences were observed in the 2- and 3-year OS rates (65.9 vs. 57.6%, P=0.001; and 44.7 vs. 36.4%, respectively; both P<0.001).

Nieuwenhuizen *et al* (39) conducted a systematic review and meta-analysis of multiple therapies, including MWA, RFA, irreversible electroporation and stereotactic ablative body radiotherapy, for the treatment of medium-sized (3-5 cm) unresectable CRC liver metastases. However, despite the fact that various studies have described long-term disease control, an insufficient number of studies were identified that directly compared these therapies and therefore no firm conclusions could be drawn. Franzese *et al* (40), in their study on CRC liver metastases, found that SBRT and MWA were associated with similar disease control effects for small lesions, whereas the use of SBRT led to an improvement in the control of lesions >30 mm. In the present study, no significant differences were identified between the two treatments when the diameter was >20 mm (P=0.426). However, when the diameter was ≤20 mm or ≤10 mm, MWA was found to be superior to SBRT in terms of local control (≤20 mm, P=0.037; and ≤10 mm, P=0.016, respectively).

For patients with lung metastases, there are clear benefits associated with the implementation of local therapy, which can be provided in a variety of modalities. Markedly higher local control of smaller lesions in RFA treatment and MWA is effective for local control on the large lesions (21). This was confirmed in the present study. When the diameter was >20 mm, the local control rate in the MWA group was 71.4%; when the diameter was ≤20 mm, the local control rate was 70.9%; when the diameter was ≤10 mm, the local control rate was 76.3%. Despite the slightly lower rate of local control of large lesions, MWA still has an objective effect. Irrespective of the approach taken, localized treatment is capable of providing patients with prolonged DFS rates. Surgical resection with adequate margins provides the greatest long-term local control for operable patients, whereas patients unable to obtain surgical treatment may be treated with other modalities, such as SBRT, ablation or other modalities that provide local control. Clearly, OS for patients cannot be attributed to pulmonary ablation alone, but rather to the comprehensive management of oligometastatic disease. The majority of patients with CRC with lung metastases receive systemic adjuvant therapy following the procedure, including chemotherapy and targeted therapy. Compared with patients receiving only chemotherapy for lung metastases, those undergoing adjuvant radiotherapy or ablation were found to have significantly prolonged 3-year survival

Table VII. Univariate and multivariate analyses for disease-free survival.

	Univariate analysis		Multivariate analysis	
Variable	HR (95% CI)	P-value	HR (95% CI)	P-value
Age, ≥70 years	1.276 (0.642-2.536)	0.486		
Sex, female	0.805 (0.460-1.407)	0.446		
BMI, <18.5 or >23.9 kg/m^2	0.751 (0.440-1.282)	0.294		
Primary cancer location, colon	0.829 (0.462-1.485)	0.528		
Extrapulmonary metastases	1.967 (1.112-3.481)	0.020[a]		
Underlying diseases	1.096 (0.644-1.864)	0.736		
Preoperative emphysema	1.058 (0.546-2.050)	0.868		
Preoperative lung bullae	1.263 (0.563-2.835)	0.572		
Hilar lymphadenopathy	0.832 (0.201-3.441)	0.800		
Mediastinal lymphadenopathy	1.262 (0.306-5.204)	0.747		
Lung lobe distribution				
Right	0.652 (0.332-1.281)	0.214		
Both	0.903 (0.461-1.769)	0.767		
CEA, ≥5.0 ng/ml	1.725 (1.003-2.964)	0.049[a]		
CA19-9, ≥37.0 IU/ml	1.894 (0.957-3.749)	0.067		
CA125, ≥35.0 U/ml	1.365 (0.379-4.916)	0.620		
Treatment modality, MWA	0.432 (0.204-0.916)	0.029[a]	0.413 (0.195-0.876)	0.021[a]
Neoadjuvant therapy	0.990 (0.575-1.705)	0.971		
Preoperative targeted therapy	0.788 (0.356-1.746)	0.558		
Preoperative I-125 seed implantation	0.426 (0.104-1.751)	0.237		
Metastasis diameter >10 mm	1.195 (0.860-1.660)	0.289		
Adjacent to vessels >3 mm	0.868 (0.546-1.381)	0.551		
Adjacent to vessels >5 mm	0.907 (0.477-1.726)	0.767		
Adjacent to the bronchus >2 mm	0.839 (0.541-1.302)	0.434		
Near mediastinal pleura 10 mm	0.996 (0.621-1.598)	0.986		
Near chest wall pleura 10 mm	1.202 (0.862-1.676)	0.279		
Near pleura 0.5 mm	1.065 (0.708-1.602)	0.763		
Near interlobar pleura 10 mm	0.998 (0.681-1.462)	0.992		
Near the diaphragm 10 mm	0.857 (0.509-1.443)	0.561		
Internal features	1.511 (1.018-2.242)	0.040[a]	1.511 (1.018-2.242)	0.040[a]
Local progression	2.041 (1.449-2.875)	<0.001[a]	2.041 (1.449-2.875)	<0.001[a]
Adjuvant postoperative therapy	1.749 (0.873-3.504)	0.115		

[a]P<0.05. CEA, carcinoembryonic antigen; CA125, glycocalyx antigen 125; CA19-9, glycocalyx antigen 19-9; BMI, body mass index; SBRT, stereotactic body radiotherapy; HR, hazard ratio; CI, confidence interval.

rates (87.5 vs. 33.3%) (41). In the present study, however, no significant differences were identified in terms of the effect of postoperative adjuvant therapy on the OS rates (P=0.344).

MWA, as an interventional treatment, intrinsically involves invasiveness. Pneumothorax is one of the common complications. Yang *et al* (24) reported a very high incidence of pneumothorax (63.8%), a finding that was very similar to the present study (66.7%), although this was higher than that reported in the majority of studies (10,42). However, only 13.5% of the patients required chest drainage in the aforementioned study, a finding that was lower than that identified in our results (24.2%). In addition, pleural effusion is a prevalent complication associated with MWA, with reported incidence rates ranging from 15-45% (43). In the present study, the incidence of pleural effusion was 42.4% and the majority of cases involved small effusions that were capable of self-absorption. For SBRT, a common adverse reaction is radiation pneumonitis. Kobayashi *et al* (18), in their study on CRC lung metastases, observed grade 1 radiation pneumonitis in 22 patients (84.6%) and no patients developed pulmonary toxicity of grade ≥2. In the present study, 54 patients (63.5%) were found to have developed radiation pneumonitis (grade ≤2) following treatment, representing a lower incidence of radiation pneumonitis compared with their study.

The current study does, however, have certain limitations. First, it was a retrospective and single-center study and despite attempts to mitigate selection bias using IPTW adjustment, the results may still be influenced by such bias. Secondly, the sample

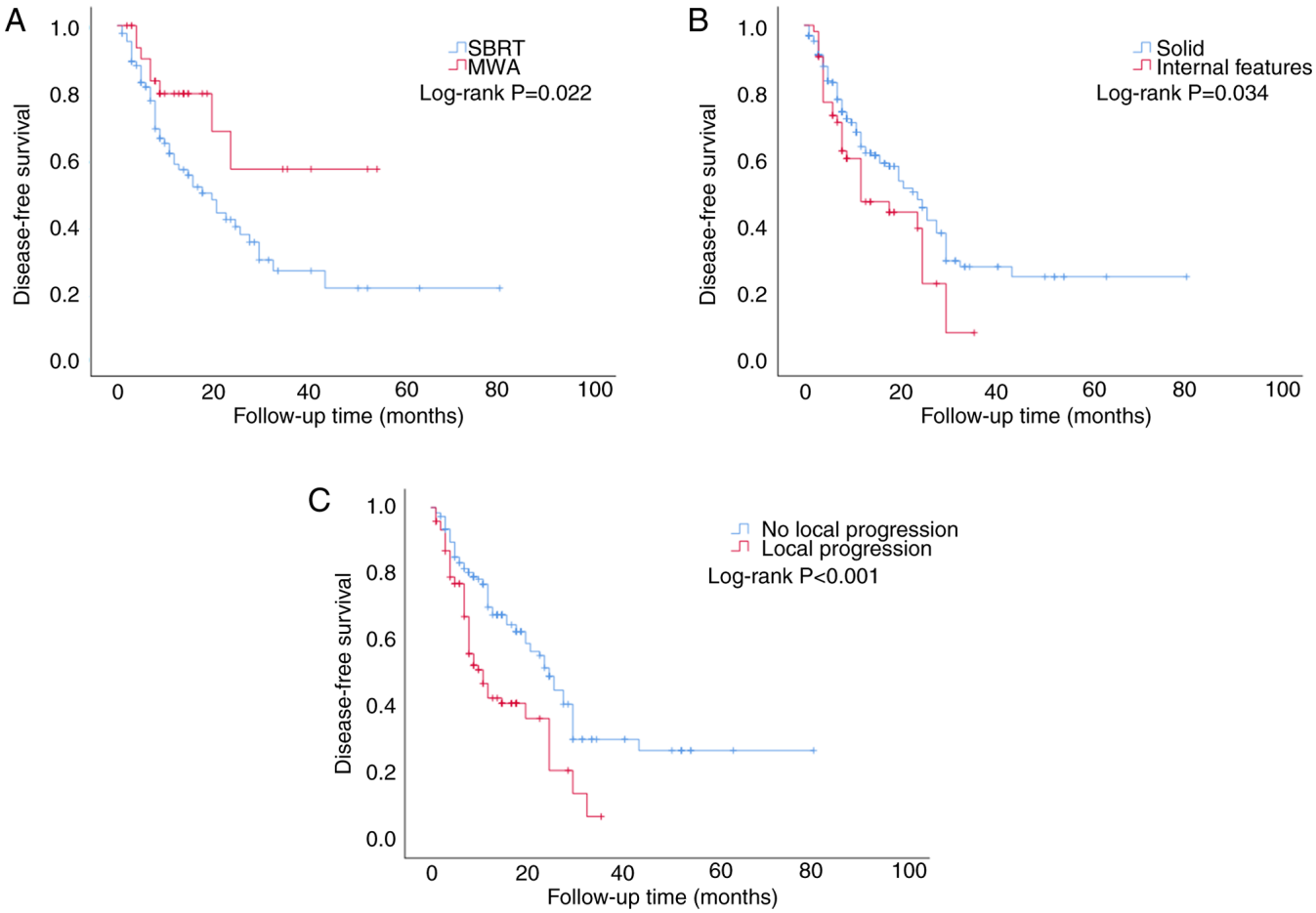

Figure 3. Kaplan-Meier method for disease-free survival. The effects of (A) treatment modality, (B) internal features of lung metastases and (C) local progression of lung metastases on disease-free survival are shown. SBRT, stereotactic body radiation therapy; MWA, microwave ablation.

size was relatively small, especially for patients undergoing MWA. Thirdly, some patients were lost to follow-up, a phenomenon that could have had an effect on the assessment of the LTPFS, RFS and OS rates. Larger-scale randomized controlled clinical trials are necessary to directly compare the efficacy of SBRT and MWA in patients with CRC with lung metastases. In addition, certain patients in the study continued to receive additional treatments, such as chemotherapy, after having been treated with SBRT or MWA. Although no significant differences were found in OS with postoperative adjuvant therapy, this cannot completely exclude the possibility of there being confounding effects on the efficacy of using SBRT or MWA alone. In addition, as the disease progresses, patients receive additional treatments to control the progression of the disease and prolong the survival, including ablation, radiotherapy, chemotherapy and so on. Although LTPFS and DFS were not affected in this study, OS was affected. When the disease progresses, patients who are treated tend to have improved OS.

In conclusion, non-surgical treatments, including thermal ablation and stereotactic body radiotherapy, are assuming an increasingly crucial role in the management of CRC lung metastases. The present study has preliminarily demonstrated that SBRT and MWA have comparable efficacy in terms of treating CRC lung metastases. However, it is worth emphasizing that MWA exhibits greater advantages in local tumor control compared with SBRT, especially when the tumor is <10 mm. Taken together, the findings of the present study may be used to provide personalized guidance for the treatment of unresectable CRC lung metastases in clinical practice.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

XW, JS, HF and TD contributed to the conception and design of the study. TD, JL, PH and YS was responsible for data collection and collation and statistical analysis. TD, JL and PH contributed to manuscript drafting and critical revisions on the intellectual content. All authors agreed to be accountable for all aspects of the work. XW, HF and TD confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

All procedures performed in the present study involving medical record information and data were approved by the Medical Ethics Committee of Sir Run Run Shaw Hospital (Zhejiang, China; project number 20230430). The requirement for informed consent was waived by the ethics committee. All methods were performed in accordance with the relevant guidelines and regulations (Declaration of Helsinki).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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