Original Article

Radiofrequency ablation versus microwave ablation for colorectal liver metastases: long-term results of a retrospective cohort surgical experience

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Background: Ablation is an alternative treatment modality for selected patients with colorectal liver metastases (CRLMs). Although initially widely performed via radiofrequency ablation (RFA), more recently, microwave ablation (MWA) is being preferred due to its perceived superiority in creating the ablation zones. The aim of this study is to compare the long-term efficacy of these two modalities performed surgically.

Methods: Patients undergoing surgical liver ablation from 2005–2023 at a tertiary center by a single surgeon for CRLM were included in a retrospective institutional review board-approved study. Outcomes were compared using Wilcoxon, Chi-square, Kaplan-Meier, and Cox multivariate regression analyses. Continuous data are presented as median (interquartile range).

Results: There were a total of 242 patients. Laparoscopic RFA was done in 121 patients with 303 lesions and laparoscopic MWA in 121 patients with 300 lesions. There was no difference between the groups regarding operative time (161 *vs.* 147 minutes, respectively, P=0.4), perioperative morbidity (3% *vs.* 8%, respectively, P=0.2) or hospital stay (1 *vs.* 1 day, P=0.05). Local recurrence (LR) per lesion with at least 1 year of imaging follow-up was 29% in the RFA and 13% in the MWA group (P<0.001). Based on univariate survival analysis, tumor size, blood vessel proximity, ablation margin, and ablation modality were independent predictors of LR. To control these variables, direct matching was performed. Each cohort included 189 lesions. Kaplan-Meier analysis of these cohorts showed increased LR-free survival in the MWA group *vs.* the RFA group (P=0.005).

Conclusions: This large study confirms our initial observation that local tumor control rate is better after MWA *vs.* RFA.

Keywords: Colorectal cancer liver metastasis; liver ablation; radiofrequency ablation (RFA); microwave ablation (MWA); local recurrence (LR)

Submitted Dec 23, 2023. Accepted for publication May 22, 2024. Published online Jul 11, 2024.

doi: 10.21037/hbsn-23-677

View this article at: https://dx.doi.org/10.21037/hbsn-23-677

Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide (1). Up to 50% of patients with CRC will develop colorectal liver metastasis (CRLM), which ultimately will drive their survival outcomes (1,2). Ten-year survival for CRLM is as low as 5% in unresectable disease (2-4). Surgical resection is the standard of care for resectable lesions, yet only 10–20% are candidates for this approach

(1,2,5,6). As such, liver tumor ablation has been utilized as an alternative in patients with unresectable disease, either due to inadequate liver remnant or comorbidities, with also a recent interest in potential curative use for small lesions (7-10). This includes such prospective trials as the COLLISION trial comparing thermal ablation to resection, and the MAVERRIC trial, performing a similar comparison for the microwave approach (10,11).

Despite the incorporation of ablation in the treatment algorithm of patients with CRLM, there are controversies in the approach (percutaneous, *vs.* surgical) and choice of technology. Ablation can be performed either percutaneously or surgically (12,13). Furthermore, the procedure can be performed using a number of different technologies, with radiofrequency ablation (RFA) or microwave ablation (MWA) technology being the most common alternatives. RFA was the first method of thermal ablation developed and utilizes alternating electrical current to generate thermal energy (13,14). This technique suffers significantly from charring and the "heat sink effect", which describes the lowering of tissue temperature with blood flow that disrupts the efficacy of the ablation process for tumors adjacent to large blood vessels. On the other hand, the newer MWA technology uses electromagnetic excitation of water molecules up to 900 MHz to create a thermal ablative effect (15). This technique may avoid the heat-sink effect (16,17). There have only been a few studies to date comparing MWA and RFA for CRLM and mostly have involved the percutaneous approach (18-22). Although used for the minority of ablations done nationally, the surgical approach has been suggested to have better local tumor control compared to the percutaneous approach (8,23,24). Therefore, it is important to investigate whether there are differences between various/ablation surgical modalities regarding outcomes.

Our previous analysis in 2018 suggested better local tumor control with MWA *vs.* RFA (21). Our aim is to compare long-term local tumor control between the two modalities using larger patient cohorts. We present this article in accordance with the STROCSS reporting checklist (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-23-677/rc).

Highlight box

Key findings
- Microwave ablation (MWA) outperformed radiofrequency ablation (RFA) in control of colorectal liver metastasis (CRLM), overall and when accounting for known confounders.

What is known and what is new?
- Although initially widely performed via RFA, more recently, MWA is being preferred due to its perceived superiority in creating the ablation zones.
- We confirm with long-term follow-up that MWA is a superior technology to RFA in the management of CRLM in a large cohort receiving surgical ablation.

What is the implication, and what should change now?
- Centers should use MWA when treating CRLM using surgical ablation.

Methods

This was a single-center retrospective cohort study at a single academic, tertiary medical center, conducted in accordance with the ethical principles of the Declaration of Helsinki (as revised in 2013). Institutional Review Board approval was obtained (Cleveland Clinic IRB#: 7820). Informed consent was waived due to the retrospective nature of the study.

Indications for ablation of CRLM at our institution and hence inclusion criteria for the current study were as follows and have been previously published by our group (13): (I) lesions that are unresectable with an inability to leave an adequate liver remnant with inflow and outflow, less than 8 in number, with total involvement of <20% of the liver; (II) patients with resectable disease, who are not candidates for surgical resection due to medical comorbidities; (III) small tumors <3 cm that would necessitate major liver resection due to their location (parenchymal preservation); (IV) joint ablation with hepatectomy to allow for curative intent resection; and (V) patients with good functional status who expressly prefer ablation to surgical resection after pros and cons are discussed objectively. Only patients undergoing initial treatment with curative intent were included in this study. The primary outcome of the study was local tumor recurrence. Secondary outcomes included complications after surgical ablation.

Patient cohorts

Patients who underwent surgical ablation for CRLM between 2005 and 2023 were identified from a prospectively maintained institutional database. Ablations were performed via RFA between 2005 and 2014 and via MWA between 2014 and 2023 by one surgeon (E.B.). Patients with at least

12 months of imaging follow-up were included in the study. Exclusion criteria were the presence of extensive extrahepatic disease not amenable to subsequent intervention (i.e., resection, ablation, external beam radiation therapy, etc.) and the presence of extensive comorbidities or debilitation rendering the patient a poor candidate for a surgical procedure under general anesthesia. In all patients, ablations were performed with a curative attempt to treat all lesions seen on preoperative imaging.

Surgical technique

The surgical technique for each approach has been described in detail before (17,19). In brief, the procedure was performed under general anesthesia, with the patients in the supine position. A laparoscopic approach was preferred except in patients undergoing combined open liver resection. For the laparoscopic approach, two 12 mm trocars were placed in the right upper quadrant, with the ablation probes being introduced through separate stab punctures in the right upper quadrant. Liver ultrasound was performed using a high-frequency rigid side-viewing transducer (Aloka, Tokyo, Japan). If the lesions were not biopsied before, a biopsy of a representative lesion was performed under ultrasound guidance using an automated biopsy gun. Then the ablation probes were taken into the field and introduced into the tumors under ultrasound guidance. Ablations were performed using the parameters described before (17,19). Most important was the monitoring of the ablation process with ultrasound to make sure the tumors were ablated with a margin by monitoring the "ablation bubbles". Overlapping ablations were performed as necessary. Ablation equipment consisted of the Angiodynamics Model 90 5 cm ablation generator used with a 150-W generator (Angiodynamics, Latham, NY, USA) for RFA and Emprint and Emprint HP systems (Medtronic, Minneapolis, MN, USA) for MWA. With both modalities, ablations were planned to create at least a cm of circumferential margin around the tumors using the standard algorithms reported before (13,25,26).

The choice of ablation only or resection plus ablation depended on the size and location of additional tumors, as well as patient preference. In those patients with bilobar tumors with a unilobar involvement of a large tumor (>3.5 cm) with or without proximity to lobar portal pedicles (in which case ablation could not be performed due to an increased risk of biliary thermal injury), a combined resection plus ablation approach was preferred. In those patients with bilobar tumors without a discrete tumor >4 cm, the decision for a laparoscopic ablation only *vs.* resection plus ablation also depended on patient preference.

The patients who underwent laparoscopic ablation only were discharged home on postoperative day (POD) 1. Those undergoing combined ablation and resection were discharged depending on clinical course, though many smaller non-anatomic wedge resections may be discharged on POD 1. A follow up liver magnetic resonance imaging (MRI) or triphasic computed tomography (CT) was obtained 1–2 weeks after ablation to rule out any incomplete ablations and repeated quarterly for the first 2 years and then biannually.

The presence of a local recurrence (LR) was diagnosed by radiologists with expertise in abdominal imaging using cross-sectional imaging including CT or MRI. Outcomes and terminologies were conducted according to the recommendations of Ahmed *et al.* (27). Only recurrence at the ablation site was considered to be LR (*vs.* those at the resection site).

Statistical analysis

The primary study outcome was the rate of LR in each group. Demographic, clinical, and procedural information from a prospectively maintained departmental database. Comparative analyses between RFA and MWA groups were conducted using Wilcoxon and Chi-square analyses. LR was analyzed using the Kaplan-Meier methods as a function over time. Parameters identified on univariate analysis with a P value <0.2 were entered into a Cox multivariate hazards model. Hazards ratios (HRs) were calculated. After the identification of the variables affecting LR other than ablation modality, direct matching of patients was performed to control the distance between matched patients on each variable separately. Matching was performed using the R software (version 4.3; Vienna, Austria). Direct matching of patients was performed to control the distance between matched patients on each variable separately. Tumor size and ablation margin, and vessel proximity were matched within 0.2 of the logits. A secondary matching approach was also included which included type of chemotherapy used in addition to the previously mentioned variables. Statistical analyses were performed using JMP software (version 17.1.0, Cary, NC, USA). A P value <0.05 was considered statistically significant for all tests. Continuous variables were presented as medians with interquartile ranges. Categorical variables were presented as

Table 1 Demographic and clinical details of study patients split by ablation modality

Parameter	RFA	MWA	P value
N (patients/lesions)	121/303	121/300	
Age (years)[a]	62 [16]	61 [16]	0.12
Sex (male/female)	77/44	75/46	0.79
Body mass index (kg/m^2)[a]	29.7 [9.4]	28 [7.7]	0.09
Tumor size (cm)[a]	1.7 [1.5]	1.2 [0.8]	<0.001
Tumor size ≥2 cm, n [%]	101 [33.3]	69 [23.0]	0.001
Number of tumors per patient[a]	2 [2]	2 [2]	0.10
Liver segmental location[&], n [%]			0.20
Anterolateral	136 [45]	156 [52]	
Posterosuperior	165 [54]	142 [47]	
Segment I	2 [1]	2 [1]	
Blood vessel proximity (near/away)[b]	130/173	161/139	0.008
Parenchymal location (superficial/deep)	165/138	176/124	0.30
Perioperative chemotherapy[c], n [%]			0.28
None	23 [19]	34 [28]	
5-FU	5 [4]	7 [6]	
FOLFOX/FOLFIRI/capecitabine	35 [29]	34 [28]	
Biological agents	58 [48]	46 [38]	

[a], median [IQR]; [b], blood vessel proximity: lesions in direct contact with or abutting a vessel measuring at least 4 mm were considered near a large blood vessel, and otherwise away; [c], perioperative chemotherapy indicates patient received chemotherapy within 6 months prior to or 12 months after the ablation procedure. [&], posterosuperior location indicates segments 4A, 7, 8; anterolateral indicates segments 2, 3, 4B, 5, 6. RFA, radiofrequency ablation; MWA, microwave ablation; 5-FU, 5-fluorouracil; FOLFOX, folinic acid, 5-fluorouracil, oxaliplatin; FOLFIRI, folinic acid, 5-fluorouracil, irinotecan; IQR, interquartile range.

frequencies and percentages.

Results

There were 121 patients (50%) who underwent RFA of 303 lesions and 121 patients (50%) MWA of 300 lesions. In the RFA *vs.* MWA groups, respectively, the procedures were laparoscopic in 99% (n=120) *vs.* 68% (n=82) and open in 1% (n=1) *vs.* 32% (n=39) of patients. The discrepancy was related to a higher percentage (40% *vs.* 10%) of the cases being done in combination with liver resection in the MWA *vs.* RFA group, respectively. *Table 1* shows a summary of the patients in each group. Both groups were similar in terms of age and sex. The number of tumors was similar in each group, and median [interquartile range (IQR)] tumor size was 1.7 (1.5) cm in the RFA group and 1.2 (0.8) cm in the MWA (<0.001). There was a higher percentage of lesions close to >3 mm vessels in the MWA (54%) *vs.* the RFA group (43%) (P=0.008). There was no difference in the rate of superficial *vs.* deep lesions in the RFA (165/138) *vs.* MWA (176/124) groups (P=0.3). The groups were similar regarding the receipt of chemotherapy. For ablation-only procedures, operative times were similar, but total ablation time was shorter [median 11.5 (IQR =13) *vs.* median 33.5 (IQR =29) minutes] in the MWA *vs.* RFA group (P<0.001). There was no incidence of postoperative incomplete ablation on postoperative CT and MRI scans. Perioperative outcomes of the patients are given in *Table 2* and Appendix 1.

Median hospital stay for laparoscopic ablation-only procedures was 1 (IQR =0) in both groups (P=0.05). Complications occurred with a similar rate in each group (P=0.14) and included urinary retention (n=1), colonic

Table 2 Perioperative outcomes of the study patients

Parameter	RFA	MWA	P value
Surgical approach (laparoscopic/open)	120/1	82/39	<0.001
Total ablation time (min)[a]	33.5 [29]	11.5 [13]	<0.001
Ablation margin (cm)[a]	1 [0.8]	1.2 [0.8]	<0.001
Total operative time (min)[a,b]	143 [78]	130 [86]	0.24
Hospital stay (day)[a,b]	1 [0]	1 [0]	0.05
90-day complications[b], n [%]	3/90 [3]	4/51 [8]	0.14
Follow-up (months)[a]	40 [46]	30 [16]	0.01
Local recurrence per lesion, n [%]	89/303 [29]	39/300 [13]	<0.001
New liver recurrence, n [%]	90/121 [74]	64/121 [53]	<0.001
Extrahepatic recurrence, n [%]	79/121 [65]	61/121 [50]	0.02

[a], median [IQR]; [b], laparoscopic ablation only. RFA, radiofrequency ablation; MWA, microwave ablation; IQR, interquartile range.

serosal tear (n=1), and pneumonia (n=1) in the RFA group (3%) and portal vein thrombosis (n=1), respiratory insufficiency (n=1), acute kidney injury (n=1), wound infection (n=1), and perihepatic fluid collection (n=1) in the MWA group (8%). One episode of bleeding requiring re-operation was peripheral in the liver and inaccessible by radiologic-guided embolization.

The median follow-up was 40 months in the RFA group and 30 months in the MWA group. The overall LR rate per lesion was 29% in the RFA group and 13% in the MWA group (P<0.001).

On univariate analysis, parameters affecting LR were ablation modality (P<0.001), tumor size (P<0.001), blood vessel proximity (P=0.001), and ablation margin (P<0.001) (*Table 3*). Kaplan-Meier survival plots for these parameters are shown in *Figure 1*. On multivariate analysis, independent predictors of LR were RFA (HR 1.97, P<0.001), tumor size ≥2 cm (HR 2.55, P<0.001), blood vessel proximity (HR 1.87, P<0.001) and ablation margin <0.5 cm (HR 2.60, P<0.001) (*Table 4*).

Direct matching was performed with tumor size and ablation margin matched within 0.3 cm and vessel proximity. Kaplan-Meier analysis for local progression-free survival time showed increased survival in the MWA group *vs.* the RFA group (P=0.005). A second matching approach replaced the vessel proximity variable with perioperative chemotherapy type, maintaining a match within 0.3 cm for both tumor size and ablation margin. Kaplan-Meier analysis for local progression-free survival in this cohort was similarly increased in the MWA *vs.* the RFA group (P=0.02) (*Figure 2*). Survival analysis for the estimated 5-year local progression-free survival in this cohort was 83% (standard error =3%) in the MWA *vs.* 72% (standard error =4%) the RFA group (log-rank test χ^2=5.3, P=0.02). Characteristics of both match cohorts are given in *Table 5*.

Discussion

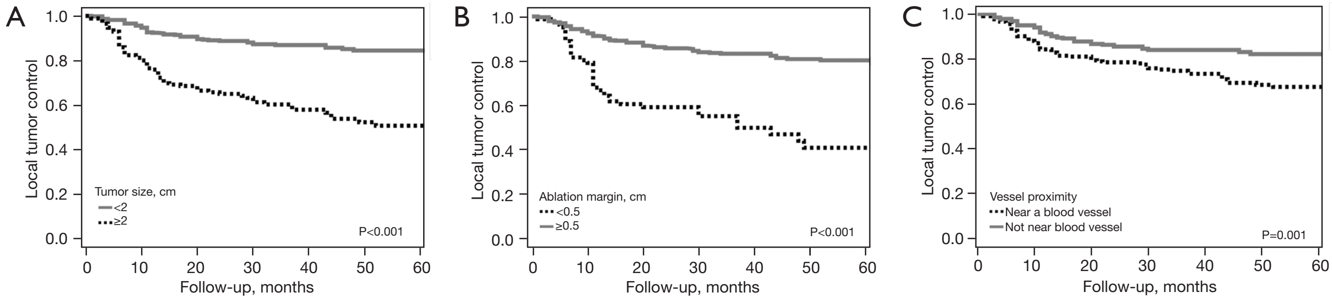
To our knowledge, this is the largest study comparing radiofrequency and MWA in the management of colorectal cancer liver metastasis and providing long-term data. The findings of this large study support our initial observation (19) that MWA provides better long-term tumor control of CRLM compared to RFA. Furthermore, MWA achieved these results by shortening the ablation time by 60% without increasing complications.

RFA was embraced with significant enthusiasm in the early 2000s (13,24,28,29) and may have even been over-utilized, as "all of a sudden, a treatment option was available" for patients who were deemed not candidates for resection. Nevertheless, the realization that local treatment failures were seen in up to 40% of tumors (25,26), advancement in resection techniques with two-staged hepatectomies, associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) and hepatic arterial infusion (HAI) pump placements, led to a significant aversion of RFA in patients with CRLM (30). Furthermore, efforts in advancing RFA technology were also placed on halt after developing 5 cm catheters (31). Then, a significant interest in microwave technology has

Table 3 Univariate analysis of factors affecting local tumor recurrence in patients with at least 12 months follow-up

Variable	LR No. (per lesion)	LR rate (%)	Median LTP-free survival length (months)*	P value†
Age				0.05
<65 years	65/357	18.20	Undefined	
≥65 years	63/246	25.60	Undefined	
Sex				0.65
Male	84/392	21.40	Undefined	
Female	44/211	20.90	Undefined	
Liver segmental location&				0.95
Anterolateral	62/292	21.20	Undefined	
Posterosuperior	65/307	21.20	Undefined	
Modality				<0.001
RFA	89/303	29.40	Undefined	
MWA	39/300	13	Undefined	
Tumor size				<0.001
<2 cm	58/433	13.40	Undefined	
≥2 cm	70/170	41.20	Undefined	
Ablation margin				<0.001
<0.5 cm	40/81	49.40	37	
≥0.5 cm	88/522	16.90	Undefined	
Blood vessel proximity				0.001
Near	78/291	26.80	Undefined	
Away	50/312	16	Undefined	
Parenchymal location				0.51
Superficial	77/341	22.60	Undefined	
Deep	51/262	19.50	Undefined	
Perioperative chemotherapy type				0.22
None	44/168	26.20	Undefined	
5-FU	1/17	5.90	Undefined	
FOLFOX/FOLFIRI/capecitabine	25/121	20.70	Undefined	
Biological agents	38/297	12.80	Undefined	

Perioperative chemotherapy indicates patient received chemotherapy within 6 months prior to or 12 months after the ablation procedure. *, Kaplan-Meier analysis; †, log-rank test; &, segment 1 lesions were excluded. LR, local recurrence; LTP, local tumor progression; RFA, radiofrequency ablation; MWA, microwave ablation; 5-FU, 5-fluorouracil; FOLFOX, folinic acid, 5-fluorouracil, oxaliplatin; FOLFIRI, folinic acid, 5-fluorouracil, irinotecan.



No. at risk	0	12 months	24 months	36 months	48 months	60 months
<2	433	401	303	195	134	86
≥2	170	130	89	54	41	23

No. at risk	0	12 months	24 months	36 months	48 months	60 months
<0.5	81	55	39	24	16	9
≥0.5	522	476	353	225	155	103

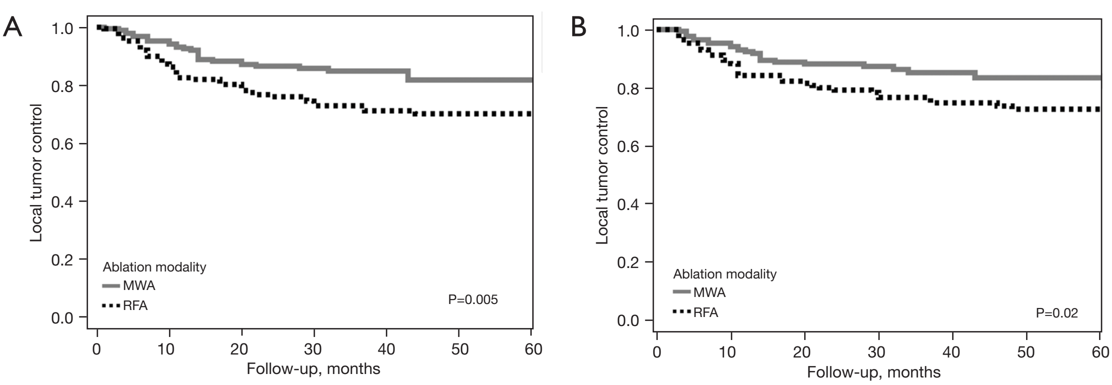
No. at risk	0	12 months	24 months	36 months	48 months	60 months
Near a blood vessel	291	245	174	119	82	60
Not near blood vessel	312	296	218	130	90	55

Figure 1 Survival analysis for variables affecting local recurrence free survival, limited to patients with at least 1-year follow-up. (A) Kaplan-Meier analysis demonstrating a significant improvement in local recurrence-free survival for ablation of lesions <2 cm in size across modalities compared with lesions ≥2 cm in size (P<0.001). (B) Kaplan-Meier analysis demonstrating a reduced local recurrence-free survival with an ablation margin <0.5 *vs.* ≥0.5 cm (P<0.001). (C) Kaplan-Meier analysis demonstrating a reduced local recurrence-free survival in lesions that are close to a major intrahepatic vessel compared with those that are not (P=0.001).

Table 4 Multivariate Cox regression analysis of factors affecting time to local recurrence per lesion using a cox-regression model

Variable	HR	95% CI	P value*
Age (≥65 *vs.* <65 years)	1.24	0.91–1.68	0.17
Modality (RFA *vs.* MWA)	1.97	1.33–2.91	<0.001
Tumor size (≥2 *vs.* <2 cm)	2.55	1.77–3.70	<0.001
Blood vessel proximity (near *vs.* away)	1.87	1.30–2.68	<0.001
Ablation margin (<0.5 *vs.* ≥0.5 cm)	2.60	1.76–3.84	<0.001

*, significant to P<0.05. HR, hazard ratio; CI, confidence interval; RFA, radiofrequency ablation; MWA, microwave ablation.



No. at risk	0	12 months	24 months	36 months	48 months	60 months
MWA	189	176	141	77	47	27
RFA	189	156	105	86	67	41

No. at risk	0	12 months	24 months	36 months	48 months	60 months
MWA	171	159	129	69	39	23
RFA	171	144	102	86	68	41

Figure 2 Local recurrence free survival after ablation of CRLM. (A) Kaplan-Meier analysis of the direct matching groups controlled for tumor size, ablation margin, and vessel proximity, showing increased local recurrence-free survival for lesions treated with MWA *vs.* RFA (P=0.005). (B) Kaplan-Meier analysis of the direct matching groups controlled for tumor size, ablation margin, and exact perioperative chemotherapy type, showing increased local recurrence-free survival for lesions treated with MWA *vs.* RFA (P=0.02). MWA, microwave ablation; RFA, radiofrequency ablation; CRLM, colorectal liver metastasis.

Table 5 Comparisons within the matched datasets

Characteristic	Overall	MWA	RFA	P value[a]
Matched on tumor size, ablation margin (both within 0.3 cm), and vessel proximity	N=378	N=189	N=189	
Tumor size (cm), mean (SD)	1.45 (0.86)	1.45 (0.86)	1.45 (0.86)	0.98
Ablation margin (cm), mean (SD)	1.09 (0.54)	1.09 (0.53)	1.09 (0.54)	0.94
Vessel proximity, n [%]				>0.99
Near a blood vessel	186 [49]	93 [49]	93 [49]	
Not near a blood vessel	192 [51]	96 [51]	96 [51]	
Matched on tumor size, ablation margin (both within 0.3 cm), and exact chemo type	N=342	N=171	N=171	
Tumor size (cm), mean (SD)	1.40 (0.85)	1.40 (0.85)	1.40 (0.84)	0.99
Ablation margin (cm), mean (SD)	1.11 (0.54)	1.12 (0.55)	1.10 (0.54)	0.76
Perioperative chemo, n [%]				>0.99
None	56 [16]	28 [16]	28 [16]	
5-FU	4 [1.2]	2 [1.2]	2 [1.2]	
FOLFOX/FOLFIRI/capecitabine	102 [30]	51 [30]	51 [30]	
Biological agents	180 [53]	90 [53]	90 [53]	

Perioperative chemotherapy indicates patient received chemotherapy within 6 months prior or 12 months after the ablation procedure. [a], Welch two-sample *t*-test, Fisher's exact test, Pearson's Chi-squared test. MWA, microwave ablation; RFA, radiofrequency ablation; SD, standard deviation; 5-FU, 5-fluorouracil; FOLFOX, folinic acid, 5-fluorouracil, oxaliplatin; FOLFIRI, folinic acid, 5-fluorouracil, irinotecan.

evolved, which has many theoretical advantages over RFA, in terms of the creation of ablation zones with faster and more homogenous heating to higher tissue temperatures that are less susceptible to the heat sink effect. Works by Shady *et al.* (18) and additional works in peri-vascular locations have specifically demonstrated this advantage (13,32). In 2015, the publication of an 8.9% LR with MWA for CRLM by Leung *et al.* (33) diverted a lot of attention to MWA to be favored as the ablation modality for CRLM. Around the same time, we also switched to MWA as our ablation modality of choice for treating malignant liver tumors.

A number of studies have compared MWA and RFA in the treatment of CRLM. For example, Correa-Gallego reported a matched cohort of patients undergoing surgical MWA and RFA, showing a benefit of MWA, though the unequal follow-up and smaller volume limited eventual conclusions (21). Bonne *et al.* demonstrated similar findings using the percutaneous technique, though this study did focus on the management of very advanced, otherwise unresectable tumors (34). The Bonne study also raised a concern regarding a higher complication rate with MWA, though the findings in our study would not support this conclusion in the surgical cohort. Additional smaller studies by Krul *et al.* and a preliminary study by our own group support similar findings (19,35). This manuscript represents the largest comparison between RFA and MWA for the surgical ablation of CRLM, supporting previous literature in finding that MWA offers improved local tumor control without the introduction of significantly higher complication rates. Certain references including Correa-Gallego did not stratify local disease control by ablation margins assessed via the same methodology which limits comparison. It has been very well shown that ablation margin is of the utmost importance in preventing LR specifically in CRLM (36-38). A margin up to 1 cm has been suggested as improving outcomes further, and we emphasize a recommendation that, at minimum, 5 mm margins should be achieved, with greater margins encouraged (39). We attempted to account for this issue using propensity score matching (PSM) to prevent confounding bias but also acknowledge that comparison of our findings to other studies is also limited by this issue. It would be ideal to have a more rigorous assessment of ablation margin than intraoperative ultrasound. However, this is a retrospective study over many years and different technologies, thus additional information is not available.

For both RFA and MWA, the success of the procedure depends first on a complete coverage of the tumor by the ablation zone. This is done by monitoring the hyperechoic ablation zones under ultrasound. If any portion of the tumor is not covered by the ablation bubbles, an overlapping ablation needs to be done. Second, a wide ablation margin should be obtained with the ablation. The larger the ablation margin, the less the risk of LR. Therefore, for CRLM, which is the most notorious tumor type regarding its treatment response, a wide ablation margin, at least >0.5 cm circumferentially should be obtained, as allowed by surrounding vasculature and biliary structures.

Parameters affecting LR in this study are in line with the literature (9,13,17,19,20,29). Tumor size was again an independent predictor of LR. Recent literature has focused on tumors smaller than 3 cm as the best indication for ablation (10,11). In fact, prospective randomized studies comparing ablation and resection have focused on this size range as a realistic target (10,11). Nevertheless, our results show a striking difference in the local control rate for tumors smaller than *vs.* larger than 2 cm for both RFA (20% *vs.* 45%) and MWA (7% *vs.* 32%). Therefore, we suggest that for CRLM that is amenable to resection, but ablation is chosen for various reasons, 2 cm may be considered as a guiding cut-off for predicting LR. The ablation margin was 1.5 mm larger in the MWA group compared to the RFA group, which brings up the question of whether the larger ablation zone is responsible for better local tumor control in the former group. Nevertheless, the ablation modality remained an independent predictor of LR, which refuses this hypothesis. Furthermore, the differences in LR between the two groups persisted even when only those tumors smaller than 2 cm were analyzed.

This study has limitations. Most notable is the retrospective fashion of the comparison, which naturally introduces the potential for between-group bias. We attempted to account for this with multi-variate analysis, and sub-analysis stratified in groups of known confounders, though it cannot totally overcome these limitations. All ablations in this study were performed by one surgeon, an approach which offers benefits and limitations. While this limits possible confounding of different technical operators, it also may limit the broader applicability of the study findings. RFA and MWA were performed in two different eras, and thus other medical advances also introduce potential between-group confounders. This could notably include new oncologic treatments, though we do attempt to account for this by reporting no differences in neoadjuvant therapy (both overall use and type of therapy employed). The difference in concurrent hepatectomy in the MWA group represents our increasingly aggressive treatment as our group became more comfortable with these approaches. However, it also introduces bias, which we attempted to account for in analyzing the complication rate also in the ablation-only cohort. There are additional differences between the two eras compared in the study, including the introduction of ALPPS and more effective chemotherapy regimens in the latter part of the study. Nevertheless, we believe that we accounted for these potential flaws as we have not incorporated ALPPS into our practice routinely and patients were matched based on the type of chemotherapy received in each group. Molecular data, such as KRAS status, was also not used to select patients for ablation therapy in either era. Still, there was a difference in surgeon experience between the groups, as MWA procedures were started 9 years after RFA. MWA was conducted open more frequently, which does make the procedure technically easier. However, by performing PSM that accounted for ablation margin, we attempted to prevent technical ease from confounding the study outcome. It would be important to consider the potential impact of genomic markers such as KRAS, though these were not available for a large proportion of patients especially earlier in the study and thus could not be meaningfully included. Follow-up was shorter in the MWA group despite being temporally later in the course; we do not have a clear cause for this. Finally, there are newer techniques using 3D CT or MRI for assessment of ablation zone that would enhance assessment of this factor (40,41). However, this technology is not available in our center, and the proper imaging for such was not available in all patients earlier in the study period, thus this technology cannot be employed in this study.

Conclusions

In conclusion, this large study shows that, when performed surgically, MWA is superior to RFA in achieving local tumor control for CRLM. It is also more efficient, by shortening ablation time by 60%. Furthermore, the data shows that a cut-off of 2 cm, rather than 3 cm is more realistic to optimize surgical oncologic outcomes by yielding an LR rate <10%. The ablation margin is the only parameter that the surgeon can impact to optimize outcomes and should be at least 0.5 cm to optimize local tumor control.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROCSS reporting checklist. Available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-23-677/rc

Data Sharing Statement: Available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-23-677/dss

Peer Review File: Available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-23-677/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-23-677/coif). E.B. reports consulting fees for consulting work from Medtronic, Ethicon and Fluoptics. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study complied with the Declaration of Helsinki (as revised in 2013). Institutional Review Board approval was obtained (Cleveland Clinic IRB#: 7820). Informed consent was waived due to the retrospective nature of the study.

References

1. Engstrand J, Nilsson H, Strömberg C, et al. Colorectal cancer liver metastases - a population-based study on incidence, management and survival. BMC Cancer 2018;18:78.
2. Adam R, De Gramont A, Figueras J, et al. The oncosurgery approach to managing liver metastases from colorectal cancer: a multidisciplinary international consensus. Oncologist 2012;17:1225-39.
3. Van den Eynde M, Hendlisz A. Treatment of colorectal liver metastases: a review. Rev Recent Clin Trials 2009;4:56-62.
4. Wang J, Li S, Liu Y, et al. Metastatic patterns and survival outcomes in patients with stage IV colon cancer: A population-based analysis. Cancer Med 2020;9:361-73.
5. Hackl C, Neumann P, Gerken M, et al. Treatment of colorectal liver metastases in Germany: a ten-year population-based analysis of 5772 cases of primary colorectal adenocarcinoma. BMC Cancer 2014;14:810.
6. Rees M, Tekkis PP, Welsh FK, et al. Evaluation of long-term survival after hepatic resection for metastatic colorectal cancer: a multifactorial model of 929 patients. Ann Surg 2008;247:125-35.
7. Groeschl RT, Gamblin TC, Turaga KK. Ablation for hepatocellular carcinoma: validating the 3-cm breakpoint. Ann Surg Oncol 2013;20:3591-5.
8. Groeschl RT, Pilgrim CH, Hanna EM, et al. Microwave ablation for hepatic malignancies: a multiinstitutional analysis. Ann Surg 2014;259:1195-200.
9. Mimmo A, Pegoraro F, Rhaiem R, et al. Microwave Ablation for Colorectal Liver Metastases: A Systematic Review and Pooled Oncological Analyses. Cancers (Basel) 2022;14:1305.
10. Puijk RS, Ruarus AH, Vroomen LGPH, et al. Colorectal liver metastases: surgery versus thermal ablation (COLLISION) - a phase III single-blind prospective randomized controlled trial. BMC Cancer 2018;18:821.
11. Tinguely P, Ruiter SJS, Engstrand J, et al. A prospective multicentre trial on survival after Microwave Ablation VErsus Resection for Resectable Colorectal liver metastases (MAVERRIC). Eur J Cancer 2023;187:65-76.
12. Zytoon AA, Ishii H, Murakami K, et al. Recurrence-free survival after radiofrequency ablation of hepatocellular carcinoma. A registry report of the impact of risk factors on outcome. Jpn J Clin Oncol 2007;37:658-72.
13. Takahashi H, Berber E. Role of thermal ablation in the management of colorectal liver metastasis. Hepatobiliary Surg Nutr 2020;9:49-58.
14. Lu DS, Raman SS, Limanond P, et al. Influence of large peritumoral vessels on outcome of radiofrequency ablation

of liver tumors. J Vasc Interv Radiol 2003;14:1267-74.
15. Martin RC, Scoggins CR, McMasters KM. Microwave hepatic ablation: initial experience of safety and efficacy. J Surg Oncol 2007;96:481-6.
16. Alonzo M, Bos A, Bennett S, et al. The Emprint™ Ablation System with Thermosphere™ Technology: One of the Newer Next-Generation Microwave Ablation Technologies. Semin Intervent Radiol 2015;32:335-8.
17. Berber E. Laparoscopic microwave thermosphere ablation of malignant liver tumors: an initial clinical evaluation. Surg Endosc 2016;30:692-8.
18. Shady W, Petre EN, Do KG, et al. Percutaneous Microwave versus Radiofrequency Ablation of Colorectal Liver Metastases: Ablation with Clear Margins (A0) Provides the Best Local Tumor Control. J Vasc Interv Radiol 2018;29:268-275.e1.
19. Takahashi H, Kahramangil B, Kose E, et al. A comparison of microwave thermosphere versus radiofrequency thermal ablation in the treatment of colorectal liver metastases. HPB (Oxford) 2018;20:1157-62.
20. van Tilborg AA, Scheffer HJ, de Jong MC, et al. MWA Versus RFA for Perivascular and Peribiliary CRLM: A Retrospective Patient- and Lesion-Based Analysis of Two Historical Cohorts. Cardiovasc Intervent Radiol 2016;39:1438-46.
21. Correa-Gallego C, Fong Y, Gonen M, et al. A retrospective comparison of microwave ablation vs. radiofrequency ablation for colorectal cancer hepatic metastases. Ann Surg Oncol 2014;21:4278-83.
22. Radosevic A, Quesada R, Serlavos C, et al. Microwave versus radiofrequency ablation for the treatment of liver malignancies: a randomized controlled phase 2 trial. Sci Rep 2022;12:316.
23. Musick JR, Gaskins JT, Martin RCG. A meta-analysis and systematic review of the comparison of laparoscopic ablation to percutaneous ablation for hepatic malignancies. Int J Clin Oncol 2023;28:565-75.
24. Mulier S, Ni Y, Jamart J, et al. Local recurrence after hepatic radiofrequency coagulation: multivariate meta-analysis and review of contributing factors. Ann Surg 2005;242:158-71.
25. Erten O, Li P, Gokceimam M, et al. Impact of ablation algorithm versus tumor-dependent parameters on local control after microwave ablation of malignant liver tumors. J Surg Oncol 2021;123:179-86.
26. Takahashi H, Kahramangil B, Berber E. Local recurrence after microwave thermosphere ablation of malignant liver tumors: results of a surgical series. Surgery 2018;163:709-13.
27. Ahmed M, Solbiati L, Brace CL, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria--a 10-year update. Radiology 2014;273:241-60.
28. Ayav A, Germain A, Marchal F, et al. Radiofrequency ablation of unresectable liver tumors: factors associated with incomplete ablation or local recurrence. Am J Surg 2010;200:435-9.
29. Buell JF, Thomas MT, Rudich S, et al. Experience with more than 500 minimally invasive hepatic procedures. Ann Surg 2008;248:475-86.
30. Abdalla EK, Vauthey JN, Ellis LM, et al. Recurrence and outcomes following hepatic resection, radiofrequency ablation, and combined resection/ablation for colorectal liver metastases. Ann Surg 2004;239:818-25; discussion 825-7.
31. Berber E, Siperstein AE. Laparoscopic Radiofrequency Ablation of Liver Tumors. In: Radiofrequency Ablation for Cancer: Current Indications, Techniques, and Outcomes. Ellis LM, Curley SA, Tanabe KK, Editors. Springer New York: New York, NY; 2004:77-88.
32. Neizert CA, Do HNC, Zibell M, et al. Three-dimensional assessment of vascular cooling effects on hepatic microwave ablation in a standardized ex vivo model. Sci Rep 2022;12:17061.
33. Leung U, Kuk D, D'Angelica MI, et al. Long-term outcomes following microwave ablation for liver malignancies. Br J Surg 2015;102:85-91.
34. Bonne L, De Paepe K, Fotiadis N, et al. Percutaneous radiofrequency versus microwave ablation for the treatment of colorectal liver metastases. J Clin Oncol 2018;36:401.
35. Krul MF, Gerritsen SL, Vissers FL, et al. Radiofrequency versus microwave ablation for intraoperative treatment of colorectal liver metastases. Eur J Surg Oncol 2022;48:834-40.
36. Calandri M, Yamashita S, Gazzera C, et al. Ablation of colorectal liver metastasis: Interaction of ablation margins and RAS mutation profiling on local tumour progression-free survival. Eur Radiol 2018;28:2727-34.
37. Wang X, Sofocleous CT, Erinjeri JP, et al. Margin size is an independent predictor of local tumor progression after ablation of colon cancer liver metastases. Cardiovasc Intervent Radiol 2013;36:166-75.
38. Leblanc F, Fonck M, Brunet R, et al. Comparison of hepatic recurrences after resection or intraoperative radiofrequency ablation indicated by size and topographical characteristics of the metastases. Eur J Surg Oncol 2008;34:185-90.
39. Puijk RS, Dijkstra M, van den Bemd BAT, et al. Improved

Outcomes of Thermal Ablation for Colorectal Liver Metastases: A 10-Year Analysis from the Prospective Amsterdam CORE Registry (AmCORE). Cardiovasc Intervent Radiol 2022;45:1074-89.
40. Vasiniotis Kamarinos N, Gonen M, Sotirchos V, et al. 3D margin assessment predicts local tumor progression after ablation of colorectal cancer liver metastases. Int J Hyperthermia 2022;39:880-7.
41. Laimer G, Jaschke N, Schullian P, et al. Volumetric assessment of the periablational safety margin after thermal ablation of colorectal liver metastases. Eur Radiol 2021;31:6489-99.

Cite this article as: Sarioglu AG, Wehrle CJ, Akgun E, Ibrahimli A, Bena JF, Berber E. Radiofrequency ablation versus microwave ablation for colorectal liver metastases: long-term results of a retrospective cohort surgical experience. HepatoBiliary Surg Nutr 2024;13(5):759-770. doi: 10.21037/hbsn-23-677