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Original Article

Comparison of surgical and percutaneous ablation methods in hepatic metastases from colorectal cancer

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Abstract: Objective: This study aims at comparing surgical resection and thermal ablation methods in the treatment of hepatic metastases from colorectal cancer in terms of relapse, survival and other parameters. Methods: Patients that underwent surgery (Group 1) and patients that underwent thermal ablation (Group 2) due to liver metastasis from colorecal cancer between the years 2008 and 2019 were included in the study. Demographic features, clinicopathologic features, average survival and progression-free survival times of patients were compared between the groups. Results: Group 1 consisted of 86 patients and Group 2 consisted of 48 patients. The average age was higher in Group 1 (60 vs. 55 years, P: 0.029) and female sex ratio was higher in Group 2 (32% vs. 52%, P: 0.021). Single metastatic tumor was predominant in Group 1 (32.6% vs. 18.8%, P: 0.0001). Metachronous tumors were higher in number in Group 2 (16.3% vs. 70.8%, P: 0.0001). Duration of hospital stay was longer in Group 1 (13.86 vs. 2.75 days, P: 0.0001). Average survival was similar to that in Kaplan Meier survival estimates (47.7 vs. 45.7 months, P: 0.336). The progression-free survival rate especially in year 5 was lower in the thermal ablation group (59.2% vs. 24.3%). And in the currrent clinical picture, the number of survivors was higher in Group 1 (75.6% vs. 56.3%, P: 0.032). Conclusions: Surgical resection should remain as the primary therapy for the treatment of hepatic metastases from colorectal cancer in appropriate patients.

Keywords: Colorectal cancer, metastasis, resection, thermal ablation and prognosis

Introduction

Colorectal cancer (CRC) is an important health problem today. It ranks the 3rd among the most frequent malignancies in terms of frequency and is one of the leading causes of cancer-related deaths [1]. Approximately 1.2 million people are estimated to contract cancer each year and 600,000 people are are estimated to lose their lives for this reason every year [1-3]. In the presence of distant organ metastasis, patients with CRC have a limited chance of long term survival. The target organ of distant organ metastasis is the liver. Liver metastasis is detected in about 25% of the patients when the disease is first diagnosed and about half of the patients develop metastasis in the course of the disease [4-7].

Although studies indicating that curative resection is the treatment modality that has the best effect on long term survival in the presence of liver metastasis from colorectal cancer (LMCRC) are available in the literature, thermal ablation methods are also among alternative methods used in the treatment of LMCRC. Five-year survival rate with R0 resection is 35-60%, and ten-year survival rate does not exceed 25% [4-7]. Only 10-20% of patients are eligible for hepatic resection. 50-70% of patients develop recurrence after curative resection [8, 9]. Despite these ratios, curative resection is the best treatment option today and has a positive effect on disease-free survival when performed in combination with preoperative chemotherapy [4-7, 10].

Different treatment modalities have been identified for the patient population that is not eligible for hepatic resection (80-90%). Administration of advanced neoadjuvant chemotherapy renders many patients resectable [11-13].

Interventional procedures targeting metastasis such as radiofrequency ablation (RFA) and microwave ablation as well as multiagent chemotherapy, biological agents are some of the treatment options that have been well accepted lately [14-18]. Thermal ablation methods are effective in the local curative treatment of unresectable and/or small hepatic metastasis from colorectal cancer [19-21]. Although RFA and microwave ablation methods are similar to each other, RFA uses electric current whereas microwave ablation uses radiofrequency energy. RFA and MWA can be performed effectively on tumors that are 3 cm or smaller in size [14-21]. General survival rate of patients with hepatic metastasis from colorectal cancer that underwent the microwave ablation method was found out to be 35.2-41.0% [22-25].

In this study, we aimed to compare surgical resection and thermal ablation methods in patients with liver metastasis from colorectal cancer in terms of recurrence, survival and other parameters, and to analyze factors that affect progression-free survival.

Materials and methods

Study design, patient selection, grouping

86 patients that underwent surgery (Group 1) and 48 patients that underwent thermal ablation (Group 2) due to hepatic metastasis from colorectal cancer at Çukurova University General Surgery Clinic and Çukurova University Interventional Radiology Clinic between the years 2008 and 2019 were included in the study. The patients were analyzed retrospectively. Approval of Çukurova University Medical Faculty Ethical Committee was obtained (01/02/2019-85/5). Since the study was retrospective, we could not get patient informed consent. Cases with liver metastasis with no colorectal cancer and cases with no adenocarcinoma were excluded from the study. Age (year in which the patient was diagnosed with primary tumor); sex; ASA (American Society of Anesthesiologists) physical status scores; neoadjuvant and adjuvant chemotherapy and radiotherapy administration; primary tumor localization; primary tumor surgery type; pathological tumor, nodes, metastases stage of the primary and metastatic tumor according to American Joint Committee on Cancer (AJCC); resection status of the primary and metastatic tumor (R0, R1, R2), presence of extrahepatic metastasis, CEA (carcinoembryogenic antigen) at the time of diagnosis of the primary tumor; location, number, synchronous-metachronous status of the metastatic tumor; type of resection performed; presence of recurrent resection; surgical complications; hospitalization duration; length of follow-up; postoperative mortality and morbidity values were recorded.

Resection of less than 2 segments was considered as a minor resection and resection of more than 2 segments was considered as a major resection.

Imaging was performed with preoperative computed tomography (CT) and/or magnetic resonance imaging (MRI). Gadoxetic acid was used in MRI as the IV intravenous contrast agent to detect small metastatic lesions. The selected patient group was given a positron emission tomogprahy (PET-CT) scanning.

Surgical method

Performance of curative resection in all operations was aimed at. Absence of extrahepatic metastasis, functional reserve status of the remaining liver (over 30% was aimed at), performance of resection with an adequate margin of surgical resection of over 1 cm, and metastases with an anatomical location and size that are suitable for resection, were taken as criteria in terms of performance of the surgery (**Figure 1**).

Intraoperative ultrasound imaging was performed after laparatomy to detect small metastases not visible through preoperative imaging methods and to detect the neighbourhood of such lesions with vascular structures. The clam-crush technique was employed in the resection of the parenchyma. The vascular access and billary tract were ligated employing clipping and suture techniques.

Thermal ablation method

RFA or MWA procedures were performed percutaneously with IV sedation or general anaesthesia accompanied by ultrasonography (USG) or computed tomography-mostly USG-after the appropriate patient position was ensured. Whereas Covidien Cool-Tip ablation system was

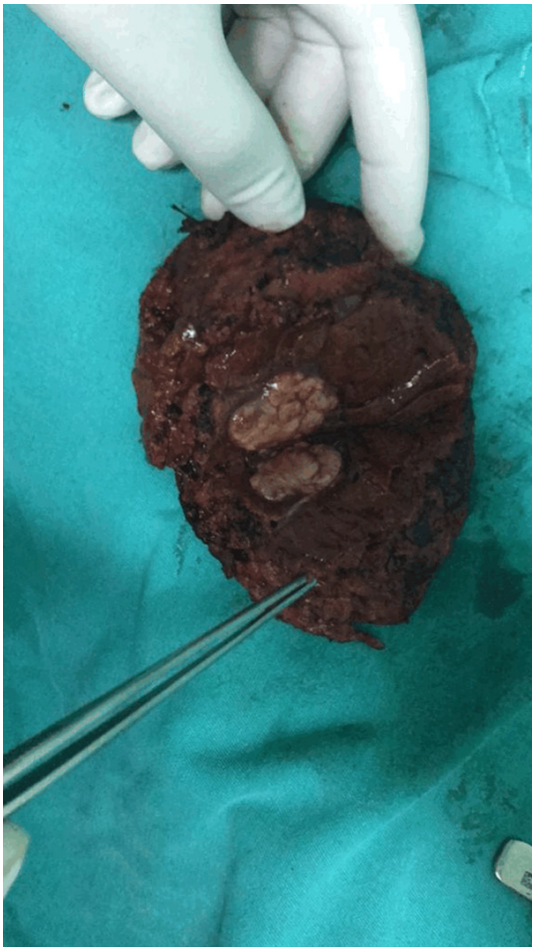

Figure 1. Segmentectomy material with liver segment 6 located colorectal cancer liver metastasis.

employed in RFA procedures, 915 Mhz Medwaves AveCure or MicrothermX, 2450 Mhz Medtronic Emprint Ablation systems were used in MWA procedures. Patients were followed up at the hospital for minimum 24 hours after all procedures. Medications thereof for IV antibiotherapy and pain palliation were planned in the meantime. The patients were discharged from hospital after they were prescribed with oral antibiotics after the inspection of their liver function tests and after their routine MRI or CT scans were planned (**Figures 2**, **3**).

Patient follow-up

Patients were followed up quarterly following the liver metastasis surgery in year 1 and once every 4 months following the liver metastasis surgery in year 2 with USG and CT; once every 6 months following liver metastasis surgery with a CT in year 3 and once a year following liver metastasis surgery with a CT in years 4 and 5. After the year 5, the patients were followed up with a USG once a year.

Statistical analysis

SPSS (Statistical Package for the Social Sciences) 23.0 program was used in the statistical analysis of the data. Categorical measurements were summarized in numbers and percentages, whereas continuous measurements were summarized as mean and standard deviation (median and minimum-maximum when required). Whereas Pearson Chi-square test statistic was employed in the comparison of categorical variables, the logistic regression method was employed in multivariate evaluations. The Shapiro-Wilk test was used in identifying whether the parameters in the study displayed normal distribution. Distributions were controlled in the comparison of continuous measurements between the groups. Independent student t-test was employed for parameters displaying a normal distribution and Mann-Whitney U test was employed for parameters not displaying a normal distribution. Kaplan-Meier analysis and Log Rank tests were used in the survival analysis. Statistical significance level was accepted as 0.05 for all tests.

Results

Demographic and clinical features

Eighty-six patients that underwent surgery (Group 1) and 48 patients that underwent thermal ablation (Group 2) were included in the study. In terms of demographic features, the average age was higher in Group 1 (60 vs. 55 years, P: 0.029), whereas female sex ratio was higher in Group 2 (32% vs. 52%, P: 0.021). Carcinoembryogenic antigen (CEA) level was observed to be higher in Group 1 (306 vs. 24, P: 0.033). Cases that underwent neoadjuvant chemoradiotherapy (NACRT) were identified to be more frequent in Group 1 (20.9% vs. 6.3%, P: 0.027). Above-mentioned outcomes relating to the groups are shown in (**Table 1**).

Tumor features

Primary tumor sizes were similar in both groups (P: 0.441). In terms of location of the primery

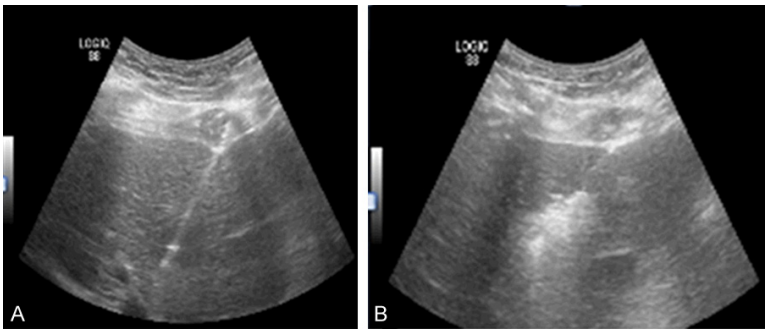

Figure 2. Ultrasonography image of the tumor. A. MW ablation probe with ultrasonography is located in the metastatic lesion. B. The appearance of the same lesion on USG after ablation.

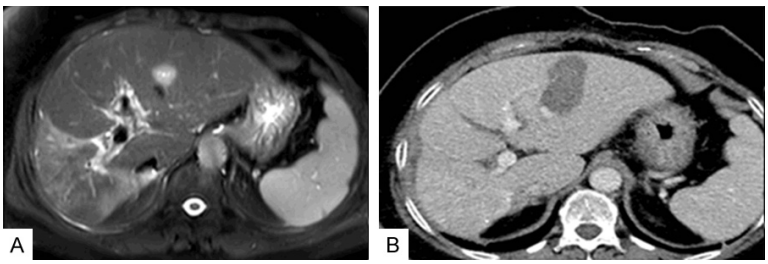

Figure 3. Radiological view of the tumor. A. Segment 2 metastatic tumor in MR before ablation. B. CT image 1 week after ablation. The tumor appears to be totally ablated.

Table 1. Demographic and clinical features

	Group 1		Group 2		P
	n	%	n	%	
Age	86	60.6±13.8	48	55.3±11.7	0.029
		62 (23-72)		57.5 (26-76)	
Sex					
F	28	32.6	25	52.1	0.021
M	58	67.4	23	47.9	
CEA	86	306.93±906.63	48	24.03±36.02	0.033
		32 (0.44-6620)		7.13 (0.67-173.2)	
NACRT					
No	68	79.1	45	93.8	0.027
Yes	18	20.9	3	6.3	

Independent student t-test, Pearson Chi-square test and Mann-Whitney U test were used. NACRT: Neoadjuvant chemoradiotherapy. CEA: Carcinoembryonic antigen. Values are presented as mean ± SD Median (Min-Max).

tumor in colorectal cancer, the tumor was predominantly located in the rectum in both groups (43% vs. 58.3%, P: 0.027). Whereas occurrence of single metastatic tumor was higher in Group 1 (32.6% vs. 18.8%, P: 0.0001), incidence of metachronous tumor was higher in Group 2 (16.3% vs. 70.8%, P: 0.0001). Tumors displayed bilobar distribution in both groups (51.2% vs. 66.7%, P: 0.059). Extrahepatic metastasis was more frequent in Group 2 (17.4% vs. 29.2%, P: 0.088). Standardised Uptake Values (SUV-max) were observed to be similar (14.62 vs. 14.21, P: 0.864). These results are shown in (**Table 2**).

Pathological and clinical features

T stage of the tumors of primary CRC were frequently in the surgical group (T4: 72.1%), and the incidence of lymp node metastasis was 68.6%. The most common complications following colorectal surgery were wound site infection (4.7%) and anastomotic leakage (2.3%). R0 resection rate in the surgery for metastasis was observed to be 71%. These outcomes are shown in (**Table 3**). The ablative procedure was performed on 41 patients in the thermal ablation group with 2450 MHZ generators and on 7 patients in the thermal ablation group with 915 MHZ generators. Average number of ablative procedures performed on the patients was 2 (1-5).

Hospitalization duration was observed to be longer in Group 1 (13.86 vs. 2.75 days, P: 0.0001). Average lengths of follow-up were similar (17.89 vs. 23.89 months, P: 0.078). Incidence of patients receiving adjuvant chemotheraphy was observed to be similar (41.9% vs. 47.9%, P: 0.310). At the end of the followup period, survival rate was higher in Group 1 (75.6% vs. 56.3%, P: 0.032). The results are shown in (**Table 4**).

Variables such as the treatment modality employed and the number of tumors were included in the analysis of independent risk factors

Table 2. Tumor features

	Group 1		Group 2		P
	n	%	n	%	
Primary Tumor Size (cm)	4.12±2.67		3.74±1.11		0.441
	3.56 (1-20)		3.51 (2.16-6.16)		
Primary Tumor Localization					
Right Colon	21	24.4	13	27.1	0.027
Left Colon	28	32.6	7	14.6	
Rectum	37	43.0	28	58.3	
Number of Metachronous Tumors					
1	28	32.6	9	18.8	0.0001
2	6	7.0	18	37.5	
>2	52	60.5	21	43.8	
Metachronous/Synchronous					
Metachronous	14	16.3	34	70.8	0.0001
Synchronous	72	83.7	14	29.2	
Metastatic Tumor Lobe					
Right	29	33.7	9	18.8	0.182
Left	12	14.0	8	16.7	
Right-Left	45	52.3	31	64.6	
Total Size of Metastatic Tumors (mm)					
<100	27	31.4	44	91.7	0.0001
>100	59	68.6	4	8.3	
Bilobar-Unilobar Metastasis					
Bilobar	45	51.2	31	66.7	0.059
Unilobar	41	48.8	17	33.3	
Extrahepatic Metastasis					
No	71	82.6	34	70.8	0.088
Yes	15	17.4	14	29.2	
Lesions treated with SUV-Max	20	14.62±9.25	48	14.21±8.88	0.864
		12.3 (3.73-40.39)		11.25 (2-37.2)	

Pearson Chi-square test and Mann-Whitney U test were used. Values are presented as mean ± SD Median (Min-Max).

that affect mortality during the multivariate logistic regression analysis. Number of metastatic tumors >2 was an independent risk factor for mortality. The results are shown in (**Table 5**).

In the average survival analysis carried out, there was not a statistical difference between the groups (P: 0.336). With regard to progression-free survival, 5-year survival rate in particular was observed to be lower in the thermal ablation group (59.2% vs. 24.3%). Results of the survey analysis are shown in (**Table 6**; **Figures 4** and **5**).

Discussion

Although a head-to-head comparison is not ideal as the characteristics of the patients are different from each other, this study provides the outcomes of different treatment modalities in LMCRC cases. An objective evaluation was carried out by including the number of metastatic tumors and the treatment modality employed in the multivariate analysis. Five-year progression-free survival rate was observed to be lower in the group that underwent thermal ablation than in the group that underwent surgery.

Rate of incidence of liver metastasis in colorectal cancer, which is a frequent malignancy globally, is around 40-50%. Resection is the most effective treatment type in the presence of hepatic metastasis from CRC and 5-year survival reaches up to 30-60% with resection [4-7]. Previous studies showed that average

Table 3. Pathological and clinical features of the group that underwent surgical treatment

	n	%
Primary Tumor T Stage		
T1	1	1.2
T2	5	5.8
T3	18	20.9
T4	62	72.1
Primary Tumor Lymph Node Metastasis		
No	27	31.4
Yes	59	68.6
Colorectal-Metastasis Same Operation		
Yes	34	39.5
No	52	60.5
ASA Score		
1	38	44.2
2	39	45.3
3	9	10.5
Single-Recurrent Resection		
Single	80	93.0
Recurrent	6	7.0
Complication Colorectal Surgery		
No Complications	72	83.7
Wound Site Infection	4	4.7
Anastomotic Leakage	2	2.3
Myocardial Infarction	2	2.3
Postoperative Bleeding	2	2.3
Sepsis	2	2.3
Liver Failure	1	1.2
Pneumonia	1	1.2
Metastasis Pathology		
R0	61	71
R1	11	12.7
R2	14	16.3

Pearson Chi-square test was used. ASA: American Society of Anesthesiologists.

survival time for cases that could not undergo resection or any other treatment was 8-10 months and chance of 5-year survival was less than 5%. Average survival time is approximately 20-24 months thanks to chemotherapeutic agents and goal-directed new treatment strategies [7, 26].

Minimal invasive techniques devoted to hepatic metastasis from CRC, transarterial chemoembolization (TACE) and thermal ablation methods have been frequently used for the past two decades. TACE is used in unresectable metastasis and in the paliative treatment of cases that will not be able to tolerate resection [27]. Thermal ablation techniques, on the other hand, have become one of the main treatment strategies that can ensure a cure for metastatic cases and RFA is one of the more frequently used alternatives. It can be as effective as resection in single lesions that are smaller than 3 cm. Again, it is a better treatment option for lesions that are deeply located in the liver and are difficult to access and resect via a surgical technique [28, 29].

When compared to the RFA method, the microwave ablation (MWA) method ensures faster local heat transfer and has a broader ablation effect. Probes holding the capacity to decrease the size of larger tissues in a shorter period of time can be used in MWA. In contrast with RFA, tip of the MWA probe is not affected by charred and dried tissues due to active heating and thus, a more favorable and reliable ablation zone can be formed [30]. The most important problem with the thermal ablation methods that have a wide range of areas of usage due to low mortality and morbidity rates is that they carry a high risk of local recurrence (39%) in lesions that are bigger than 3 cm in particular [20, 31]. A difference between RFA and MWA that was significant in terms of overall survival and ablation site recurrence could not be found during literature review in a series of studies comparing RFA and MWA for colorectal liver metastases (CRLM) consisting of 243 patients (P=0.559 and 0.078, respectively). However, the rate of complication was observed to be higher in the group that underwent MWA due to peribiliary CRLM (P=0.002) [32]. Yet, in another study, recurrence rates that were lower than those in the group that underwent RFA were observed in the group that underwent MWA (6% vs. 20%, P<0.01) [33].

As is revealed by various non-randomized comparative studies, resection is recognized as a gold standard treatment type as against systemic therapy in the treatment of patients with colorectal liver metastasis (CRLM) [34]. Patients with tumors that are unresectable through surgical treatment in the beginning can undergo downstaging by receiving neoadjuvant chemotherapy. Segmental resection, lobectomy, two stage hepatectomy such as associating liver partition and portal vein li-

Table 4. Outcomes

	Group 1		Group 2		P
	n	%	n	%	
Hospitalization Duration (Days)	86	13.86±8.25	48	2.75±2.96	0.0001
		11 (4-34)		2 (1-15)	
Length of Follow-Up (Months)	86	17.89±14.04	48	23.89±24.72	0.078
		14 (0-69)		16 (1-97)	
Adjuvant Chemotherapy					
No	36	41.9	23	47.9	0.310
Yes	50	58.1	25	52.1	
Current Status					
Live	65	75.6	27	56.3	0.032
Ex	21	24.4	21	43.8	

Pearson Chi-square test and Mann-Whitney U test were used. Ex: Exitus values are presented as mean ± SD Median (Min-Max).

Table 5. Risk factors affecting mortality

	B	S.E.	Wald	df	P	Odds Ratio	95% C.I. for Odds Ratio	
							Lower	Upper
Surgical	-0.506	0.426	1.409	1	0.235	0.603	0.262	1.390
Number of Metachronous Tumors 1 (ref.)			7.473	2	0.024			
Number of Metachronous Tumors >2	-1.742	0.639	7.438	1	0.006	0.175	0.050	0.613
Number of Metachronous Tumors =2	-0.785	0.516	2.316	1	0.128	0.456	0.166	1.254
Constant	0.686	0.222	9.575	1	0.002	1.986		

Logistic regression was used. Method: Backward: Wald CI, confidence interval.

tigation for staged hepatectomy (ALPPS) and other resection options can be performed on tumors that were rendered resectable thanks to neoadjuvant chemotherapy. Alternative minimal invasive treatment types such as radiofrequency ablation (RFA) and microwave ablation (MWA) are being increasingly used on patients that are considered to be unresectable despite all the above-mentioned techniques. Employment of these methods has led to some problems such as survival and recurrence and these issues have been analysed in many studies [14, 23, 28, 35].

International guides approach thermal ablation treatment with caution and emphasize the significance of correct patient selection. While firm recommendations are not available in The American College of Radiology (ACR) guide, radiofrequency ablation was announced not to be eligible for the treatment of CRLM. However, no adequate scientific evidence is available in the guide for such statement [36]. The US National Comprehensive Cancer Network (NCCN) guides do not offer any well-defined recommendations for RFA and MWA. Thermal ablation methods cannot be expected to totally replace resection for patients with resectable lesions. Resection or ablation are recommended for patients with lesions that are eligible for curative surgery. Surgery, ablation or combination of the two are not recommended in the local therapy for known metastatic lesions. Single treatment protocols intended for lesions as a whole are more preferable methods [37]. The guide published by UK National Institute For Health and Care Excellence (NICE) states that the use of thermal ablation for unresectable lesions or on patients that have previously undergone hepatic resection is more appropriate [38]. The European Society for Medical Oncology (ESMO) embraces thermal ablation for lesions smaller than 4 cm if surgery is contraindicated and cites the study conducted by European Organization For Research and Treatment of Cancer (EORTC)- the chemotherapy + local ablation versus chemotherapy (CLOCC) study [21, 39]. Most comprehensive recommendations are available in the guide published by Dutch Comprehensive Cancer Center (IKNL).

Table 6. Survival analyses

	Estimated Average	Standard Error	% 95 Confidence Interval For the Average		One-year progression-free survival %	Three-year progression-free survival %	Five-year progression-free survival %	P
			Limit Inferior	Limit Superior				
Overall*	47	9.8	28.8	67.2	85.9	67.9	32.3	-
Group**								
Group 1	47.7	4.0	39.8	55.6	85.8	67.7	59.2	0.336
Group 2	45.7	6.3	33.4	58.1	83.1	61.7	24.3	
Number of Metachronous Tumors**								
1	53.8	5.6	42.8	64.8	86.1	72.7	72.7	0.364
2	49.3	8.3	32.9	65.7	84.6	70.5	26.9	
>2	43.3	4.8	33.9	52.8	81.7	64.8	25.0	

*Kaplan meirer, **Log rank was used.

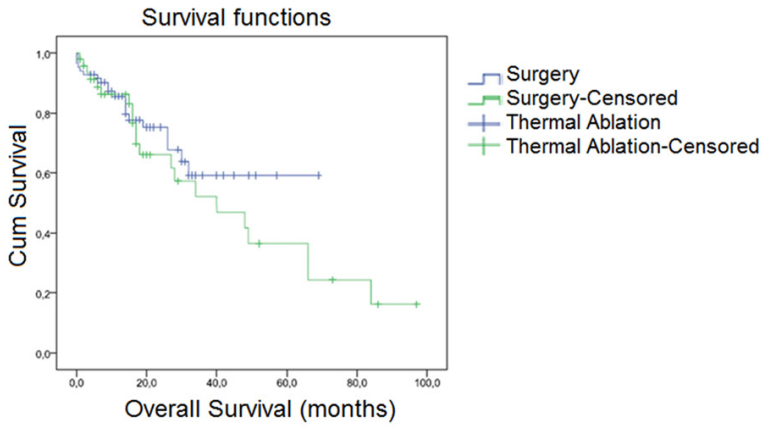

Figure 4. Overall survival time per group.

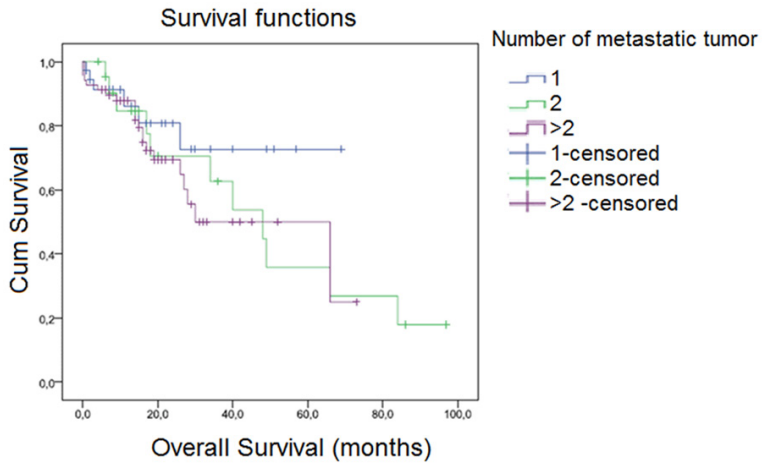

Figure 5. Overall survival time per the number of metastatic tumors.

This guide states that thermal ablation cannot replace resection but might be an eligible alternative treatment option for unresectable CRLM [40]. In conclusion, Thermal ablation methods can be consulted in cases of advanced age, comorbidity, unresectable anatomic localization, small metastatic tumors or patients that are less eligible for the surgical treatment option [41].

In the meta-analysis comparing the surgical resection and thermal ablation methods for hepatic metastasis from colorectal cancer carried out by van Amerongen et al, the average diameter of metastasis of patients that underwent thermal ablation was smaller (mean difference: -0.59; 95% CI -0.79 to -0.39; P: 0.001). The study also showed that ASA scores thereof were higher than those of the group that underwent surgical resection (mean difference: 0.21; 95% CI 0.04-0.38; P: 0.01). van Amerongen et al confirmed that patients that underwent thermal ablation received more neoadjuvant chemotherapy more frequently (P: 0.002) and ajduvant chemotherapy less frequently (P: 0.002) [35].

The study carried out by Wang et al comparing resectable hepatic metastasis from colorectal cancer showed that at the average age and sex ratio of the groups were similar and that the primary cancer was predominantly located in the colon in both groups (P: 0.802). Synchronous tumor was dominant (P: 0.277) and the lobar distribution of the metastatic tumor was similar in both groups (P: 0.076). In the study, demographic and clinical features were not related to the treatment type [42]. Many studies have revealed that the complications in surgical treatment are significantly higher than those in thermal ablation (relative risk [RR] =0.47; % 95 CI 0.28-0.78) [43].

Another study comparing hepatectomy and radiofrequency ablation for hepatic metastasis from colorectal cancer has shown that a difference with respect to the sex, age, preoperative CEA level of the patient; primary tumor location (the colon or the rectu); neoadjuvant chemotherapy; adjuvant chemotherapy; number, location, maximum diameter and TNM stage of CRLM; lymphatic invasion; vascular invasion; histological differentiation or comorbidities is not available between the groups [44].

In our study, age average of the group that underwent thermal ablation was lower and female patients were predominant. Location of the primary tumor and the lobe, in which the metastatic tumor was located, displayed similar distribution in both groups. CEA levels at the time of diagnosis of the primary tumor were observed to be higher in the group that underwent surgical treatment. Although it was observed that patients that had undergone

surgical treatment received more neoadjuvant therapy, number of patients receiving adjuvant therapy was observed to be similar in both groups. Tumor diameter was an influential factor as expected in the selection of the thermal ablation treatment. Number of metastatic tumors was associated with treatment selection and patients with a single tumor underwent a higher number of surgical treatments. Thermal ablation treatment was predominantly administered to metachronous metastases. 90% of patients that underwent surgical treatment had an ASA score of less than 3 and postoperative complications developed in 17% of the patients in the group. R0 resection could not be achieved in 29% of the patients. Hospitalization duration was distinctively longer- as expected- in the group that underwent surgical treatment. A high metastatic lymph node ratio (68.6%) in the primary tumor might be a factor that predicts development of synchronous or metachronous liver metastasis.

Meta-analysis comparing the surgical resection and thermal ablation methods in hepatic metastasis from colorectal cancer carried out by van Amerongen et al showed that the 5-year overall survival of patients in the group that underwent resection was significantly better than that of patients that underwent thermal ablation (Odds Ratio (OR) =2.35, % 95 GA=1.49-3.69, P: 0.001). Five-year disease-free survival (DFS) was found out to be significantly higher in the group that underwent resection than that of the group that underwent thermal ablation (OR=2.20, % 95 Confidence Interval (CI) =1.28-3.79, P: 0.005). When van Amerongen et al carried out a subgroup analysis of patients with solitary tumors up to 3 cm in size and patients with tumors bigger than 3 cm, thermal ablation displayed an increased odds ratio for local recurrence when compared to liver resection in both cases. van Amerongen et al showed odds ratio in the subgroups to be (OR=7.68, 95% CI 4.44-13.28, P: 0.001; and OR=8.75, 95% CI=3.38-22.64, P: 0.001), respectively [35]. There are other studies in the literature that show that surgical resection is superior to thermal ablation in terms of overall survival and disease-free survival [41, 45].

Gleisner et al performed a matched-control and propensity score analysis. Disease recurrence rate after RFA was observed more frequently in year 1 among patients undergoing resection only (66% vs. 24%; P<0.001). Gleisner et al determined recurrence rate of the ablation site after RFA (41% vs. 2%; P<0.001) to be more frequent than that in the group that underwent surgical treatment [46].

In their study comparing radiofrequency ablation and surgical resection for the treatment of resectable hepatic metastasis from colorectal cancer, Wang et al observed rates of OS in the resection and RFA groups to be similar in year 1 (97.8% vs. 95.7%), year 2 (83.6% vs. 91.3%) and year 3 (66.8% vs. 71.6%), which was different from what the literature reported. According to Kaplan-Meier analyses, median OS was 74 months in the group that underwent resection and 59 months in the group that underwent RFA (P=0.484). However, their study intrahepatic relapse (36.9% vs. 11.9%, P: 0.001) and local relapse (15.2% versus 6.5%, P: 0.099) were more frequent in the group that underwent RFA in furtherance of the literature. Hepatic relapse (69.6% vs. 32.6%, P<0.00) and systemic relapse (26.1% vs. 39.1%, P: 0.129) rates were similar in both groups [42].

In our study, overall survival in the Kaplan-Meire estimates was similar in both groups (47.7 vs. 45.7 months, P: 0.336). Although 1-year progression-free survival rate (85.8% vs. 83.1%) and 3-year progression free survival rate (67.7% vs. 61.7) were approximate, there was a significant difference in 5-year progression-free survival rates (59.2% vs. 24.3%). Number of metastatic tumors did not affect average survival (P: 0.364).

When the literature is examined, 5-year DFS and OS values were found out to be significantly lower in patients that underwent RFA than those in patients that underwent resection. This outcome is thought to be associated with a higher relapse rate in patients that underwent RFA. Furthermore, a high heterogenity exists between the calculations of DFS and OS. Possible causes of such heterogenity might be different ablation techniques, lack of definitive criteria in the selection of ablation techniques and different practices during the selection of patients. Many clinics see RFA as a treatment option in cases when the disease is unresectable due to insufficent liver paren-

chyma, localization of the tumor in an area in which the resection thereof is very difficult, comorbidity factors of the patient and presence of an extrahepatic disease. Whereas surgical failures and average survival rates are prioritized in RFA, local recurrence rate might be ignored.

Thermal ablation treatment continues developing as technology advances. As was shown in the CLOCC study, thermal ablation contributes to local control and OS in cases of unresectable diseases. Although several studies set forth the comparable outcomes of thermal ablation treatments for resectable disease compared to hepatectomy [41, 47, 48] more evidence is required to recommend ablation treatment against hepatectomy. The COLLISION study is a phase III randomized trial comparing thermal ablasion and liver resection for patients with a small (<3 cm) CRLM [43]. Another ongoing research, the LAVA study has been designed to compare liver resection and ablative treatment for patients with CRLM [49]. These recent randomized trials might give more evidence for this dilemma.

The limitation of this study is its failure to randomize patients due to its retrospective design and the different disease burdens and different oncological statuses of the patients.

Thermal ablation methods are minimal invasive methods for the treatment of CRLM, which has complication rates lower than those of liver resection. Besides, RFA is now associated with increased recurrence rates and low disease-free and general survival and therefore, it should be used only for patients that are not eligible for surgery. Due to lack of randomized trials, evidence is based on retrospective database studies with strong selection bias on the matter of eligibility for specific treatment modalities. Therefore, there is a need for randomized controlled trials looking into the primary treatment for CRLM in order to obtain objective outcomes relating to oncological survival.

Disclosure of conflict of interest

None.

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