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# Efficacy of Radiofrequency Ablation in the Treatment of Hepatic Metastases of Non-Colorectal Cancers

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**ABSTRACT:**

## Efficacy of radiofrequency ablation in the treatment of hepatic metastases of non-colorectal cancers

**Objective:** To determine the efficacy of radiofrequency ablation (RFA) method in treatment of hepatic metastases of non-colorectal cancers.

**Material and Method:** This retrospective cohort included 28 patients (17 women, 11 men) diagnosed with a total of 101 hepatic metastases of non-colorectal cancers. RFA under sonographic guidance was administered to 95 (94.1%) of lesions, while surgical resection was performed for 6 (5.9%) metastases. At the time of diagnosis, 10 (35.7%) of patients had a single lesion; whereas 18 (64.3%) patients had multiple lesions. Average number of ablated lesions was 2 (range, 1 to 6) and their average diameter was 2.4 cm (range, 0.9-5.2 cm). All patients routinely received chemoradiotherapy.

**Results:** Portal venous thrombosis and liver abscess were detected after RFA in 1 (3.5%) and 2 patients (7%), respectively. Mean duration of follow-up was 17 months (range, 1-51 months) and complete ablation was accomplished in 17 (76%) of our series. Thirteen sessions of repetitive RFA was performed in 7 cases with recurrent disease. During the follow-up period, widespread hepatic metastases and extrahepatic disease were encountered in 6 (21%) and 16 (57%) patients, respectively. Mortality occurred in 9 (32%) patients due to disseminated disease.

**Conclusion:** Our results indicate that RFA can be a promising therapeutic alternative in patients with hepatic metastasis of non-colorectal cancers, particularly breast cancer and neuroendocrine tumors. Number of lesions is the most important parameter likely to affect the overall and disease free rates of survival.

**Keywords:** Liver, metastasis, non-colorectal cancer, radiofrequency ablation, treatment

**ÖZET:**

## Kolorektal dışı kanserlerin karaciğer metastazlarında radyofrekans ablasyon yönteminin etkinliğinin değerlendirilmesi

**Amaç:** Kolorektal dışı kanserlerin karaciğer metastazlarında radyofrekans ablasyon (RFA) yönteminin tedavideki etkinliğinin değerlendirilmesi.

**Gereç ve Yöntem:** Karaciğere metastatik kolorektal dışı kanser tanısı almış, toplam lezyon sayısı 101 olan 28 hasta (17 kadın, 11 erkek) retrospektif kohort çalışmamıza dahil edildi. Çalışmamızda 95 (%94.1) lezyona ultrasonografi eşliğinde RFA uygulanırken, 6 (%5.9) lezyona cerrahi rezeksiyon yapılmıştı. Tanı anında 10 (%35.7) olguda tek lezyon, 18 (%64.3) olguda multipl lezyon bulunmaktaydı. Ablasyon yapılan ortalama lezyon sayısı 2 (1-6) ve ortalama boyut 2.4 (0.9-5.2) cm olarak belirlendi. Tüm olgular kemoradyoterapi almıştı.

**Bulgular:** RFA sonrası 1 (%3.5) olguda portal ven trombozu, 2 olguda (%7) karaciğer apsesi gelişti. Ortalama takip süresi 17 (1-51) aydı. 17 (%76) olguda ilk takipte tam ablasyon sağlandı. Rekürrens saptanan 7 olguda 13 seans reRFA uygulandı. Takipte 6 (%21) olguda yaygın hepatik metastaz, 16 (%57) olguda ekstrahepatik hastalık izlendi. 9 (%32) olgu yaygın hastalık nedeniyle kaybedildi.

**Sonuç:** Sonuçlarımız RFA'nın kolorektal dışı kanserlerin karaciğer metastazlarında, özellikle de meme kanseri ve nöroendokrin tümörlere ait metastazlarda umut verici bir tedavi alternatifi olduğunu göstermektedir. Hastalıksız ve genel sağkalımı etkileyen en önemli parametre ise lezyon sayısı olarak görülmektedir.

**Anahtar kelimeler:** Karaciğer, metastaz, kolorektal dışı kanser, radyofrekans ablasyon, tedavi

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## INTRODUCTION

Metastatic cancers comprise the vast majority of liver tumors (1). Metastasis to liver most commonly ensources from colorectal tumors (2). Else than colorectal tumors, cancers originating from bronchi, pancreas, stomach and breast may spread to liver. Contemporarily, surgical resection is the only potentially curative treatment modality for primary and secondary malignancies of liver. Even though metastasectomy can prolong survival in some cases with hepatic metastases of colorectal cancers, benefit of surgery in liver metastases of non-colorectal tumors could not be demonstrated (1).

Various interventional therapeutic modalities have been developed for treating secondary malignancies of liver such as portal vein embolization (PVE), transarterial chemoembolization (TACE) and RFA (3).

Recently use of RFA has become more and more popular in the treatment of hepatic metastases of non-colorectal tumors (1). Promising results have been reported especially in the hepatic metastases of breast cancer and neuroendocrine malignancies (4).

The aim of the present study was to assess the efficacy of RFA treatment in patients with hepatic metastases of non-colorectal tumors.

## MATERIAL AND METHODS

Approval of local Institutional Review Board and written informed consents from all participants were obtained prior to the study. This trial was implemented in accordance with principles in the Declaration of Helsinki and good clinical practice guidelines.

This retrospective cohort was carried out in the radiology department of our institution between September 2007 and June 2013. A total of 28 patients included in this study which have been selected by oncology council that is consisted of interventional radiology, medical oncology and general surgery departments. Bilobar or multifocal involvement of tumors, adjacency to major vascular or biliary structures, insufficient liver volume after surgery, co-existent morbidities and contraindications for general anesthesia were the main indications for selection of these cases.

The most common malignancies were breast (n=8, 28.6%), stomach (n=4, 14.3%) and neuroendocrine tissue (n=4, 14.3%) tumors/cancers. An overview of non-colorectal origins of hepatic metastases is presented in Table-1. Comorbidities such as congestive heart failure, hypertension, coronary artery disease and chronic renal failure were detected in six patients (21.4%). Extrahepatic metastases including lymph node, bone, brain, lung, adrenal gland, peritoneum, colon, small intestine and stomach were diagnosed in 12 cases (42.9%). These patients have been added to study for palliative causes and to prolong survival. No combined resection had been made to these patients before the procedure. Twenty-five patients (89.3%) had been operated for primary tumor prior to RFA procedure. Three patients received chemotherapy prior to RFA.

Initial evaluation for RFA was ultrasonography for determining the site, number, localization and accessibility of lesions. Findings derived from computerized tomography (CT) scans and magnetic resonance imaging (MRI) views were used for staging the disease prior to the intervention. Laboratory study for RFA candidates included complete blood count, liver and kidney function tests, liver function tests and coagulation parameters. Platelet count less than 50.000/mm$^3$ and International Normalized Ratio (INR) value greater than 1.25 were exclusion criterias. All patients were preoperatively routinely examined by anesthesiologists in terms of risks of general anesthesia.

During RFA, procedures were carried out after a fasting period of 8 hours while patients were maintained in supine or supine oblique positions according to the localization of the lesion. Thermal ablation was accomplished using RITA Starbust Talon (RITA Medical Systems Inc., California, USA) thermal ablation electrode and RITA model 1500X generator. Saline infusion was made using a pump (Intelli Flowpump, RITA Medical Systems Inc., California, USA). In order to achieve a safe and effective ablation, a necrotic area extending beyond tumor site and involving a peritumoral tissue of 1 cm diameter was aimed. Tip of the electrode was advanced under sonographic guidance and needles were placed appropriately in the target area. Sensors located in

the tips of five electrodes in the center and four quadrants allowed monitorization of heat in the tissue during the procedure. The temperature in the target tissue was adjusted as 105°C. In seven sessions applied for six patients, hydrodissection was made by 5% dextrose infusion through 18G Chiba needle (Mycomedical, North Carolina, USA) prior to thermal ablation for lesions adjacent to diaphragm, stomach, duodenum, colon and kidney. Thereby, risk for injury of these organs was reduced. The interval required for formation of an ablation areas of 2 cm, 3 cm and 4 cm were 0, 5 and 9 minutes, respectively. To prevent blurring of vision due to gas artefacts caused by tissue heat, RFA was initially applied to lesions distant to the transducer and then to the lesions near to superficial. Impedance efficiency on the generator was closely monitored during RFA. These values indicating tissue resistance against the current ranged between 1 and 10. The ideal value for the current accompanied by a low resistance was determined as 10. At the end of RFA, trocar was withdrawn at 50 W power and a target temperature of 50°C with ablative intervals of 1 cm. Just after the procedure, an ultrasonographic control was made to rule out any complications, which may occur in the early period. If no complications were noted, patients were discharged the day after RFA.

Distribution of intraoperative or percutaneous approaches for RFA in our series is demonstrated in Table-2. For follow-up, 3-phase contrast CT (Light Speed VCT, GE Medical Systems, Waukesha, WI, USA), dynamic and diffusion MRI (1.5 T, Signa Excite II, GE Medical Systems, Waukesha, WI, USA) were made 1 month after RFA.

Lack of contrast enhancement around or within tumor site at early and late (portal phase or at 5$^{th}$ minute) views, presence of a clear and well-circumscribed boundary at the site of ablation and an ablation area larger than tumor zone with respect to initial findings in CT scans were consistent with total ablation. Contrast enhancement at lesion site after RFA was interpreted as "residual tumor", whereas detection of contrast enhancement after total ablation at tumor site was termed as "local progression". Recurrence was defined as observation of new lesions. IN MRI views, lack of contrast enhancement at T1-weighted dynamic images, hypointense signals of ablated lesions at T2-weighted images, lack of diffusion restriction in diffusion sequences with high values of apparent diffusion coefficient (ADC) due to cellular necrosis in an area larger than the primary lesion were interpreted as total ablation.

Follow-up of patients were made by CT and/or MRI sections on 1st and 6th months after RFA. Follow-up modality selection was made randomly. In 19 patients (67.9%), residual, local progressive or recurrent disease were detected. These patients received a total of 13 sessions of reRFA and/or additional treatment modalities.

### Statistical Analysis

Analysis of data was carried out by Statistical Package of Social Sciences program version 11.5 (SPSS Inc., Chicago, IL, USA). Descriptive data for quantitative variables were expressed as mean±standard deviation or median-interquartile range. Discrete variables were shown as number and %. Efect of nominal variables on recurrence and survival were assessed with Kaplan-Meier method using Log-Rank test. For every variable, recurrencefree survival rates and 95% confidence intervals were evaluated at 3,6 and 12 months; while overall survival rates were calculated at 1, 3 and 5 years. Level of significance was set at $p<0.05$. Impact of discrete variables on overall and recurrence-free survival rates were evaluated with Single variable Cox Proportional Hazards regression analysis. Relative risks estimated for all variables and 95% confidence intervals were calculated. Variables likely to affect recurrence-free survival rates and risk factors were evaluated together with Multiple variable Cox Proportional Hazards regression analysis. In these analyses, variables those display p values <0.25 were further assessed in multiple variable model.

## RESULTS

A total of 28 patients (17 women, 11 men) with an average age of 56.3±9.8 (range, 38 to 79) years were included in this study.

A total of 101 lesions were taken into account in

this trial. Six (5.9%) lesions were treated with metastasectomy, while RFA was administered in 95 (94.1%) patients. At admission, a single lesion was observed in 10 (35.7%) patients, whereas 18 cases (64.3%) had multiple lesions. A total of 65 lesions were treated at initial RFA procedure. Remaining lesions were treated at second and subsequent sessions. The average number of lesions treated by RFA was 2 (range, 1 to 6). The average size of lesions was 2.4 cm while 24 (85.7%) of lesions was smaller than 4 cm. All procedures were performed by using a 3.5 mHz probe.

The average duration of follow-up in our series was 27.8 (range, 2 to 68) Months. In seven patients, a total of 31 lesions (16 recurrent, 15 residual or local progressive) received RFA. Four patients received RFA once, while two patients received RFA twice and one patient received RFA 5 times.

At the control on first month, complete ablationwas observed in the18 of 28 (64.2%) patients. Follow-up examinations indicated that mean time until occurrence of local progression or recurrence was 4 months (range, 2 to 68). In 19 patients (67.9%), intrahepatic residual or recurrent disease was determined. Sixteen patients (84.2%) displayed residual or recurrent disease within the first 6 months after RFA. In seven patients with diagnoses of residual or recurrent disease (25%), a total of 13 sessions of RFA were administered. At the end of follow-up period, three patients (10.7%) were found to be free of recurrence or extrahepatic metastases. Notably, seven patients (25%) had extrahepatic metastases without recurrent disease in the liver. In this session 11 patients (39.2%) with intrahepatic recurrence were scheduled for reRFA. Six patients (21.4%) were kept under follow-up due to disseminated hepatic metastases.

Chemotherapy, radiotherapy and hormone treatment were applied in 21 (75%) cases before or after RFA. Radioembolization was added to the treatment protocol due to intrahepatic metastases. A total of 16 patients (57.1%) revealed extrahepatic metastases including lymph nodes, adrenal gland, colon, gallbladder, lung, brain, peritoneum and small intestines (Table-1). Mortality occurred in nine

**Table-1:** Descriptive and clinical features of our series (n=28)

| Variable | |
|---|---|
| Age [mean±SD (range)] | 56.3±9.8 (38-79) |
| Gender (male/female) | 11/17 |
| Diagnosis | |
| Breast | 8 (28.6%) |
| Gastric | 4 (14.3%) |
| Neuroendocrine | 4 (14.3%) |
| Other | 12 (42.8%) |
| Comorbidity | |
| Yes | 6 (21.4%) |
| No | 22 (78.6%) |
| Extrahepatic metastases | |
| Yes | 16 (57.1%) |
| No | 12 (42.9%) |
| History of operation for primary tumor | |
| Yes | 25 (89.3%) |
| No | 3 (10.7%) |
| Additional treatment | |
| Yes | 21 (75%) |
| No | 7 (25%) |
| Metastasectomy | |
| Yes | 3 (10.7%) |
| No | 25 (89.3%) |

SD= Standard deviation

**Table-2:** Clinical features and characteristics of lesions

| Variables | n (%) |
|---|---|
| Total number of lesions | 101 (100) |
| RFA | 95 (94.1) |
| Metastasectomy | 6 (5.9) |
| Lesions treated with RFA | |
| Primary | 65 (64.3) |
| Residual/recurrent | 30 (29.7) |
| Number of RFA procedures | 41 (100) |
| Single | 28 (68.3) |
| Repeated | 13 (31.7) |
| Number of lesions [average (range)] | 2 (1-6) |
| Single | 10 (35.7) |
| Multiple | 18 (64.3) |
| Size of lesion (cm) [average (range)] | 2.2 (0.9-5.2) |
| < 4 cm | 24 (85.7) |
| ≥ 4 cm | 4 (14.3) |
| Hydrodissection with 5% dextrose | |
| Yes | 22 (78.6) |
| No | 6 (21.4) |
| Route of RFA application | |
| Intraoperative | 1 (3.6) |
| Percutaneous | 26 (92.9) |
| Intraoperative and percutaneous | 1 (3.6) |
| Follow-up modality | |
| CT | 3 (10.7) |
| MRI | 15 (53.6) |
| CT and MRI | 10 (35.7) |

RFA= Radiofrequency ablation, CT= Computerized tomography, MRI= Magnetic resonance imaging

**Table-3:** Impact of risk factors on recurrence-free survival rates (Kaplan-Meier analysis)

| Variables | Survival rate (months) | | | Duration of survival | Log rank | p Value |
|---|---|---|---|---|---|---|
| | 3 | 6 | 12 | | | |
| Gender | | | | | | |
| Male | 54.5 | 45.4 | 36.4 | 18.8 (6.2-31.4) | 0.03 | 0.856 |
| Female | 64.7 | 41.2 | 29.4 | 22.4 (8.4-36.4) | | |
| Cancer diagnosis | | | | | | |
| Breast | 62.5 | 37.5 | 25.0 | 15.7 (1.2-30.3) | 4.25 | 0.119 |
| Gastric | 25.0 | 25.0 | N/A | 2.7 (0.0-5.6) | | |
| Other | 68.7 | 50.0 | 43.7 | 31.4 (15.6-47.2) | | |
| Comorbidity | | | | | | |
| No | 59.1 | 40.9 | 27.3 | 16.5 (7.4-25.6) | 0.73 | 0.393 |
| Yes | 66.7 | 50.0 | 50.0 | 35.3 (9.2-61.5) | | |
| Extrahepatic metastases | | | | | | |
| No | 58.3 | 41.7 | 33.3 | 24.7 (7.3-42.0) | 0.00 | 0.985 |
| Yes | 62.5 | 43.7 | 31.2 | 18.5 (7.4-29.6) | | |
| Previous surgery for primary tumor | | | | | | |
| No | 100 | 100 | 66.7 | 32.3 (12.1-52.6) | 1.84 | 0.175 |
| Yes | 56.0 | 36.0 | 28.0 | 21.2 (2.8-5.2) | | |
| Overall | 60.7 | 42.9 | 32.1 | 24.0 (12.8-35.2) | - | - |
| Additional treatment | | | | | | |
| No | 85.7 | 57.1 | 42.9 | 31.9 (8.6-55.1) | 1.11 | 0.293 |
| Yes | 52.4 | 38.1 | 28.6 | 16.8 (7.3-26.4) | | |
| Metastasectomy | | | | | | |
| No | 56.0 | 40.0 | 32.0 | 18.6 (9.5-27.6) | 0.26 | 0.608 |
| Yes | 100.0 | 66.7 | 33.3 | 26.7 (0.0-59.7) | | |
| Number of applications | | | | | | |
| Single | 66.7 | 47.6 | 42.9 | 30.8 (17.0-44.6) | 3.96 | 0.047* |
| Multiple | 42.9 | 28.6 | N/A | 3.6 (1.7-5.5) | | |
| Lesion size | | | | | | |
| < 4 cm | 66.7 | 45.8 | 37.5 | 27.5 (14.9-40.0) | 2.28 | 0.131 |
| ≥ 4 cm | 25.0 | 25.0 | N/A | 3.2 (0.8-5.7) | | |
| Number of lesions | | | | | | |
| Single | 100.0 | 80.0 | 60.0 | 33.6 (19.6-47.6) | 8.17 | 0.004* |
| Multiple | 38.9 | 22.2 | 16.7 | 13.3 (2.0-24.6) | | |

N/A: Analysis not applicable, *: statistically significant

patients (32.1%). Disseminated disease (n=4, 14.2%) and deterioration of general condition (n=5, 17.8%) were responsible for mortality.

Subsequent to RFA, abscess was diagnosed in two patients (7%) and portal vein thrombosis occurred in one case (3.5%). Portal vein was followed with conservative approach, while percutaneous drainage and intravenous antibiotics were administered to patients with abscess formation. The average duration of recurrence-free survival and median life expectancy were 24 months and 4 months, respectively. 95% confidence interval was between 1.93-6.07. Recurrence free survival rates at 3 months, 6 months and 12 months were 60.7%, 42.9% and 32.1%, respectively.

Single variable analysis on recurrence free survival indicated that number of lesions (p=0.004) and number of RFA applications (p=0.047) influenced the rate of recurrence free survival. The more the number of lesions, the shorter the recurrence-free survival rate was. The average survival was 33.6 months in patients with a single lesion, while it was 13.3 months in case of multiple lesions. Similarly, increased number of RFA applications was associated with a shorter recurrence-free survival (Table-3) (Figure-1).

In contrary, gender (p=0.856), primary tumor site (p=0.119), presence of extrahepatic metastases (p=0.985), additional treatment modalities (p=0.293), size of lesion (p=0.131), previous history of metastasectomy (p=0.608) and presence of comorbidities (p=0.393) were found to be unrelated with recurrence-free survival.

Variables linked with recurrence were number of lesions, type of primary tumor and history of operation for primary tumor. Every increase in the number of

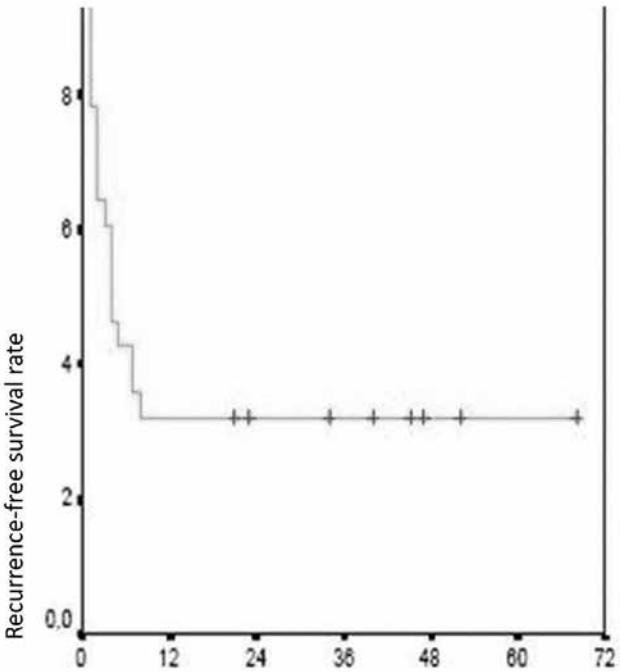


**Figure-1:** Kaplan-Meier curve demonstrating recurrence-free survival rate

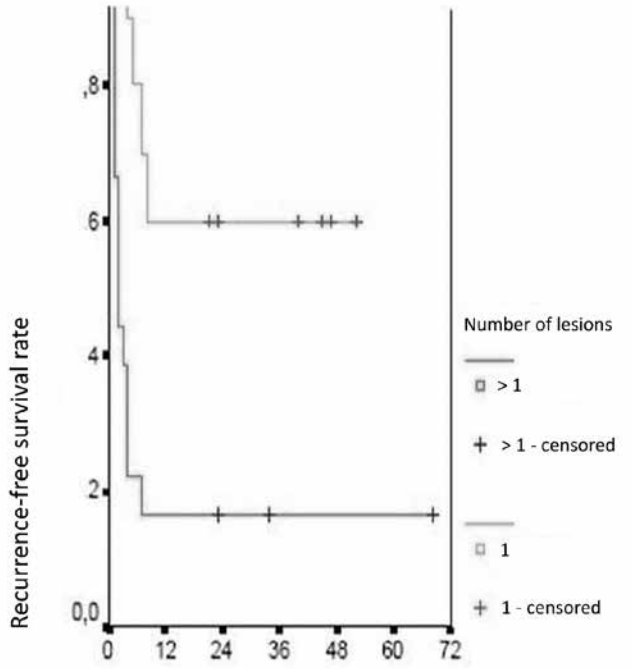


**Figure-3:** Kaplan-Meier curve indicating recurrence-free survival rate with respect to number of lesions

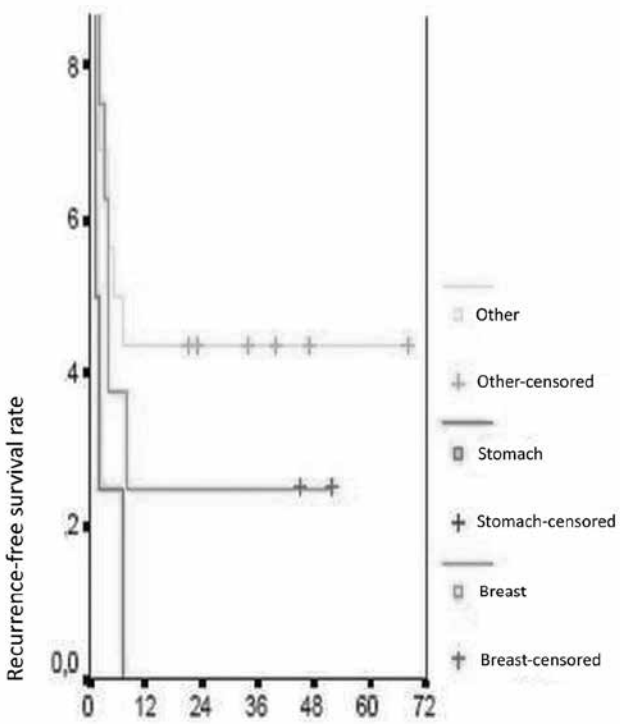


**Figure-2:** Kaplan-Meier curve indicating recurrence-free survival rate with respect to oncologic diagnoses

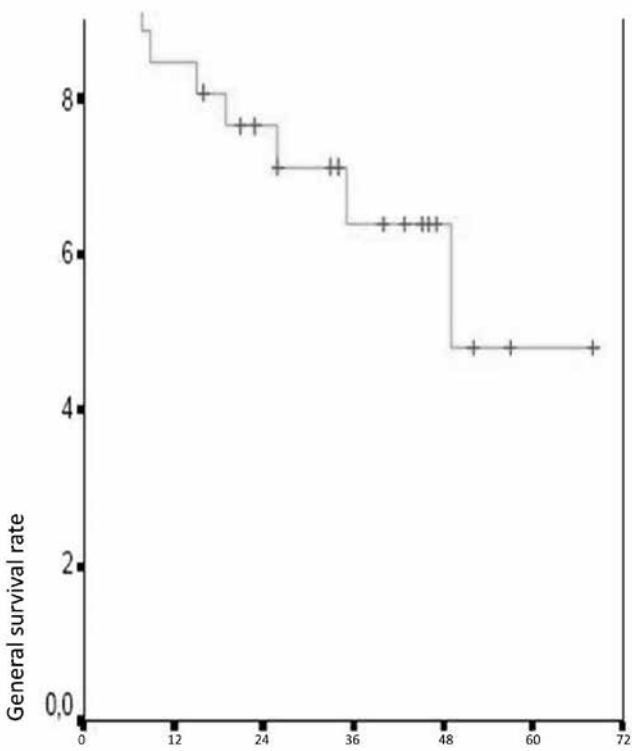


**Figure-4:** Kaplan-Meier curve indicating general survival rate for all patients

**Table-4:** Impact of risk factors on overall survival (One variable Kaplan-Meier analysis)

| Variables | Survival rate (%) | | | Duration of survival | Log rank | p Value |
|---|---|---|---|---|---|---|
| | 1 year | 3 year | 5 year | | | |
| Gender | | | | | | |
| Male | 80.8 | 70.7 | N/A | 35.8 (25.1-46.6) | 0.06 | 0.805 |
| Female | 87.4 | 64.2 | 48.1 | 47.7 (35.3-60.2) | | |
| Cancer diagnosis | | | | | | |
| Breast | 87.5 | 56.2 | N/A | 39.6 (27.7-51.4) | 0.27 | 0.873 |
| Gastric | 100.0 | N/A | N/A | 19.0 (13.5-24.5) | | |
| Other | 80.4 | 73.0 | 48.7 | 47.7 (33.8-61.6) | | |
| Comorbidity | | | | | | |
| No | 85.9 | 58.2 | N/A | 39.5 (30.3-48.7) | 0.73 | 0.394 |
| Yes | 80.0 | 80.0 | 80.0 | 56.0 (35.0-77.0) | | |
| Extrahepatic metastases | | | | | | |
| No | 91.7 | 42.8 | 42.8 | 42.8 (25.4-60.2) | 0.28 | 0.596 |
| Yes | 81.2 | 74.5 | N/A | 42.9 (32.7-53.2) | | |
| Previous surgery for primary tumor | | | | | | |
| No | 100.0 | 100.0 | N/A | N/A | 1.09 | 0.295 |
| Yes | 82.8 | 60.1 | 45.1 | 44.8 (33.2-56.2) | | |
| Overall | 84.8 | 63.9 | 47.9 | 46.7 (35.8-57.5) | - | - |
| Additional treatment | | | | | | |
| No | 83.3 | 41.7 | 41.7 | 50.2 (31.9-68.6) | 0.22 | 0.640 |
| Yes | 85.1 | 57.2 | N/A | 40.4 (30.7-50.2) | | |
| Metastasectomy | | | | | | |
| No | 83.2 | 59.5 | N/A | 37.2 (29.5-44.8) | 1.94 | 0.164 |
| Yes | 100.0 | 100.0 | 100.0 | N/A | | |
| Number of applications | | | | | | |
| Single | 79.2 | 61.1 | 40.7 | 44.5 (31.7-57.3) | 0.21 | 0.650 |
| Multiple | 100.0 | 71.4 | N/A | 45.6 (32.2-59.0) | | |
| Lesion size | | | | | | |
| < 4 cm | 86.8 | 68.3 | 51.3 | 48.5 (37.1-60.0) | 0.65 | 0.420 |
| ≥ 4 cm | 75.0 | 37.5 | N/A | 29.2(13.8-44.7) | | |
| Number of lesions | | | | | | |
| Single | 100.0 | 100.0 | N/A | N/A | 7.06 | 0.008* |
| Multiple | 76.2 | 43.1 | 21.5 | 35.0 (22.2-47.8) | | |

N/A: Analysis not applicable, *: statistically significant

lesions was associated with a 3.93 times amplified relative risk for mortality (95% confidence interval: 1.080-14.266, p=0.038). Patients diagnosed with gastric cancer (5.914 times) and a history of operation for primary tumor (47.229) were associated with increased risk for mortality (95% CI: 1.914-1165.57, p=0.018) (Figures-2 and 3).

Overall survival rates for first, third and fifth years were 84.8%, 63.9% and 47.9%, respectively. Mean life expectancy was 46.7 months (95% CI: 35.85-57.46). The only variable significantly associated with overall survival rate was number of lesions (p=0.008). Patients with single lesions had 100% overall survival in first and third years, while cases with multiple lesions exhibited survival rates of 76.2% and 43.1%, respectively. Even though number of RFA applications was negatively associated with recurrence-free survival, this factor had no impact on overall survival rate (p=0.650) (Table-4) (Figure-4).

The variable with the most prominent effect on mortality was the number of lesions. Each increment in the number of lesions brought about a 1.512 times amplified relative risk for mortality (95% CI: 1.040-2.199; p=0.030).

## DISCUSSION

Surgery constitutes the mainstay of treatment in metastatic disease limited to the liver with survival rates ranging between 20-46% (5). Efficacy of surgical resection in hepatic metastases of non-colorectal tumors is obscure compared to that of colorectal

tumor metastases.

Five-year and 10-year overall survival rates of hepatic metastases of non-colorectal malignancies including neuroendocrine tumors were 36% and 23%, respectively. In the same report, recurrence-free survival rates for 5 years and 10 years were found to be 21% and 15%; also 5 year survival rates are reported as low as 5% after chemotherapy in these patients (6). Therefore, an alternative treatment is required in patients who are inappropriate for surgery or who did not benefit from surgical treatment (5). In this context, RFA is a cheap, reliable and less invasive modality of choice.

Yun et al. (7) have assessed efficacy of RFA for hepatic metastases of non-colorectal tumors. Their results with an average duration of follow-up of 23.3 months demonstrated a complete ablation rate of 88%, mean recurrence-free survival of 10.1 months and overall survival rate of 28.8 months. Survival rates for 1, 3 and 5 years were reported as 86%, 39% and 19% (7). They reported no factors likely to affect overall and recurrence-free survival (7). In our series, rate of complete ablation was found to be 64.2% at the first follow-up. The average recurrence-free survival was 24 months, whereas overall survival rates in first, third and fifth years were 84.8%, 63.9% and 47.9%, respectively. The most important factor associated with survival was number of metastatic lesions. Our complete ablation rates were lower than Yun's series (7), however, our recurrence-free and overall survival rates were higher.

In hepatic metastases of non-colorectal tumors, surgical resection constitutes the mainstay of treatment (8,9). Nevertheless, attributed to the distinct biological characteristics of non-colorectal tumors, long-term results of surgical treatment is under debate (10).

Despite the fact that RFA treatment is not a very common method in the management of non-colorectal tumors, the present study yielded some remarkable results. Rate of 3-year survival in metastases of breast cancer to liver ranged between 50-71% and hepatic insufficiency is the main cause of death in liver metastases of breast cancer (11,12). Sofocleous et al. (13) administered 220 sessions of RFA to hepatic metastases of breast cancer and noted that recurrence-free survival was 12 months. In their series, overall survival rates in the third and fifth years were 70% and 30%. These findings remind that RFA can be a good adjunctive therapeutic option in hepatic metastases of breast cancer (13). Meloni et al. demonstrated that tumor size and the period until the diagnosis were the most important prognostic factors in hepatic metastases of breast cancer. They stated that RFA was an effective mode of treatment for these cases (14). Notably, our rates of overall and recurrence-free survival were higher than those in recent publications and similar to outcomes of surgical treatment.

Overall survival rates for surgical resection of liver metastases of gastric cancer in the first, third and fifth years were 62%, 30% and 26.5%, respectively (15). Yun et al. (7) reported that RFA provided survival rates of 78%, 22% and 0% in these cases. Radiofrequency ablation seems to be less effective than surgical resection in terms of survival, but it can be promising in terms of local tumor control. Due to high probability of local tumor recurrence in gastric cancer, RFA should be used as an additional modality for liver metastases of gastric cancer (7). In our series, recurrence-free survival rate for gastric cancer metastases to liver was 2.75 months and overall survival rate at the end of first year was 50%. Interestingly, the gastric cancer metastases to liver exhibited the worst prognosis. Aggressive course of disease and high rates of local recurrence may be responsible for this circumstance.

We noted that number of lesions and applications of RFA may influence recurrence-free survival rates. This finding may be attributed to the fact that tumors with higher potential for local recurrence necessitate an increased number of RFA applications. We performed the majority of RFA interventions (n=39, 81.25%) via percutaneous route. Percutaneous route provides a safe and practical way since it avoids risks associated with anesthesia. Analysis of our data has shown that route of RFA application did not have any significant impact on survival rates.

Berber et al. (16) demonstrated that almost half of local recurrences occurred in the first 6 months after RFA. Neuroendocrine tumors were less likely to display recurrence and lesion size was an important

parameter for recurrence. We observed that 84.2% of local recurrences occurred in the first 6 months and repeated RFA applications have been administered in 11 patients. Our results did not establish any link between lesion size and survival rate.

Our survival rates are lower than the outcomes of metastasectomy in recent publications. However, we have reported better survival rates compared to reports focusing on the efficacy of RFA. Particularly, we noted that hepatic metastases of neuroendocrine tumors are more likely to benefit from RFA either in terms of curative or palliative management.

In the present study, no extrahepatic metastases were detected while the decision for RFA was made. However, extrahepatic metastases including mainly lymph nodes were observed during follow-up in 16 patients. Our analysis has shown that presence of extrahepatic metastases in the follow-up period did not have an adverse influence on overall survival rates.

In parallel to recent publications (17,18), we advocate the use of 5% dextrose intraperitoneally for hydrodissection during RFA. In this manner, prevention of organ injury during the procedure can be achieved.

Our mortality and complication rates are comparable to similar trials (7,19). Bleeding, abscess formation and pneumothorax were most frequent complications in the literature. We came across complications in 10.5% of our series.

Main limitations of the present study are small sample size, retrospective design and heterogenity of patient group. Moreover, this data reflects the experience of a single institution.

## CONCLUSION

To conclude, results of the current study indicate that RFA is a safe, effective and minimal invasive procedure with promising results for hepatic metastases of non-colorectal tumors. It is particularly beneficial in unresectable lesions and it can provide improved survival rates. Further controlled trials on larger series can aid in making more accurate conclusions on the efficacy of this method.

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