Clinical study of radiofrequency ablation combined with TACE in the treatment of breast cancer with liver metastasis

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Abstract. We studied the clinical effects of percutaneous radiofrequency ablation (RFCA) combined with transcatheter arterial chemoembolization (TACE) in the treatment of breast cancer with liver metastasis. Eighty-eight patients with a diagnosis of breast cancer with liver metastasis for the first time and patients with liver metastasis after radical mastectomy were consecutively selected. The subjects were divided according to the different treatment methods. They were divided either into the control group of 50 cases or the observation group of 38 cases. Breast cancer patients underwent radical mastectomy with conventional systemic venous chemotherapy. The liver metastasis control group used TACE, while the observation group combined RFCA with TACE. The two groups were followed up for a median time of 20 months, and the clinical effects were compared. The effective rate of the observation group was higher than that of the control group; differences were statistically significant (P<0.05). There was no differences in the incidence of complications between the two groups (P>0.05). The progression free survival, median survival time and survival rate of the observation group were increased; differences were statistically significant (P<0.05). Therefore, RFCA combined with TACE in the treatment of breast cancer with liver metastasis is safe and effective.

Introduction

Breast cancer incidence rate ranks first in female malignant tumors. Liver metastasis in breast cancer is third only to lung and bone metastasis. The breast cancer liver metastasis rate is ~55.0-75.0%. In ~5.0-45.0% of patients, liver is the only metastatic site (1). The overall median survival period of patients with liver metastasis due to breast cancer is ~14 months. Approximately 20.0-45.0% of patients with breast cancer 5 years after radical resection have distant metastases, and 6.0-40.0% of patients have distant metastases at the time of initial diagnosis (2). The main treatments for breast cancer with liver metastasis are surgical resection, transcatheter arterial chemoembolization (TACE), percutaneous radiofrequency ablation (RFCA), ethanol injection, and microwave ablation (3,4). The safety and effectiveness of TACE and RFCA in primary hepatocellular carcinoma have been confirmed (5,6), however, due to the different molecular biological characteristics of metastatic liver cancer, there is no uniform understanding regarding whether RFCA and TACE are equally effective at present. The previous study conducted on this subject had a much lower sample size, with a lack of comparative analysis. Based on previous results, this study attempts to explain the clinical effects of both TACE and RFCA in the treatment of breast cancer with liver metastasis.

Materials and methods

Sample selection. Eighty-eight patients with a diagnosis of breast cancer with liver metastasis at Tengzhou Central People's Hospital from January 2013 to January 2016 were consecutively selected. The inclusion criteria were as follows. i) Age ≤70. ii) Diagnosis of breast cancer with liver metastasis, or breast cancer after radical surgery with liver metastasis, confirmed by pathology. This study was approved by the Ethics Committee of Tengzhou Central People's Hospital. Signed written informed consents were obtained from all participants before the study. iii) No presence of extrahepatic metastasis and liver metastases were diagnosed by ultrasound, MRI or CT, without any surgical resection indications, with TACE and RFCA application indications. iv) The KPS score ≥70, and ECOG <2, after liver function was corrected in the normal range, there was a tolerance to the risk of treatment of TACE and RFCA. v) The clinical data were perfect and the informed consent was obtained. The exclusion criteria were: i) breast cancer chemotherapy response was poor, the condition was serious, and the survival was expected to be <12 months. ii) There were serious underlying diseases, such as heart, lung, brain, kidney and other organs dysfunction, and other parts of the primary malignant tumors.

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Table I. Comparison of therapeutic effects of two groups of metastatic lesions [case (%)].

Group	No. of cases	CR	PR	SD	PD	Effective rate
Control group	50	5	27	10	8	32 (64.0)
Observation group	38	10	22	3	3	32 (84.2)
χ^2 test						4.446
P-value						0.035

Table II. Comparison of complications [case (%)].

Group	No. of cases	Bone marrow suppression	Infected	Severe digestive tract symptoms	Liver and kidney damage	Other	Complication rate
Control group	50	1	1	2	1	1	6 (12.0)
Observation group	38	1	1	1	1	0	4 (10.5)
χ^2 test							0.0002
P-value							1.000

Table III. Comparison of progression-free survival, median survival time and survival rate.

Group	No. of cases	Progression-free survival	Median survival time	Survival rate
Control group	50	5.7	11.9	25 (50.0)
Observation group	38	8.2	15.6	27 (71.1)
χ^2 test		5.967	6.324	3.959
P-value		0.008	0.003	0.047

According to the different treatment methods, the patients were divided into two groups of controls of 50 cases and the observation group of 38 cases. The average age of the control group was 56.7±14.5 years. The diagnosis of breast cancer with liver metastasis was present in 32 cases, and breast cancer after radical surgery with liver metastasis was present in 18 cases. The average diameter of breast cancer was 3.8±1.4 cm, the average number was 1.5±0.6, the average number of metastatic lymph nodes was 6.5±2.3 with the pathological type of invasive ductal carcinoma in 32 cases. There were 15 cases of small leaf cancer, and 3 other cases. There was an average of 6.2±2.5 months after radical operation with a presence of hepatic metastases. The average metastasis was 1.3±0.4, with an average maximum diameter of 3.3±1.2. The mean serum AFP was 685.7±124.6 μg/l. The average age of the observation group was 58.2±13.6 years, with the first diagnosis of breast cancer with liver metastasis in 30 cases. Breast cancer after radical surgery with liver metastasis was in 8 cases. The average diameter of breast cancer was 4.1±1.7 cm, the average number was 1.4±0.5, the average number of metastatic lymph nodes was 6.3±2.2, with a pathological type of invasive ductal carcinoma in 25 cases, 11 cases of small leaf cancer, and 2 other cases. There was an average of 5.8±2.1 months after the radical operation to hepatic metastases. The average metastasis was 1.2±0.3, average max diameter was 3.5±1.3, and the mean serum AFP was 724.5±133.8 μg/l. The baseline data in both groups were comparable.

Research methods. Breast cancer patients underwent radical mastectomy with conventional systemic venous chemotherapy. The liver metastasis control group used TACE, while the observation group combined RFCA with TACE. The intravenous chemotherapy administered was epirubicin + cyclophosphamide sequential docetaxel + trastuzumab (EC-TH) or epirubicin + cyclophosphamide followed by paclitaxel + trastuzumab (EC-PH). The TACE scheme is Changchun vinorelbine + capecitabine (NX) with or without trastuzumab (H), docetaxel + capecitabine (TX) with or without trastuzumab (H). The Seldinger method was successfully used to insert into the right femoral artery, and the catheter was selectively inserted into the hepatic artery of the celiac artery, which was injected into the hepatic artery. The tumor location, size and distribution of the blood supply were established. This was conducted according to the appropriate dose of drug injections, combined with embolization materials (Yangze Pharm, Taizhou, China). We used the Radionics radiofrequency treatment instrument and the Cool-tip radiofrequency ablation electrode needle (Johnson & Johnson, New York, NY, USA), with the exposed end of 3 cm. The ultrasound guided percutaneous ablation was inserted into the appropriate depth of the tumor with a adjustment to the maximum power. The single ablation was 10 min, multi-point ablation; by edge needle ablation methods, the ablation range completely covered the tumor to the edge of 0.5-1.0 cm. In the operation, the surgeon judged whether full ablation was completely achieved. One,

3, 6, 9 and 12 months after operation, the ultrasound, CT or MRI were performed to assess the progression and recurrence of metastatic lesions. During treatment, the condition changes were closely monitored, and the serious adverse drug reactions were observed with symptomatic treatment.

Observation index. The two groups were followed up for 6.0-35.0 months, and the median time was 20 months. The treatment effects, complications, progression-free survival, median survival and survival rate of the two groups were compared. According to the RECIST evaluation criteria in solid tumors, the lesions disappeared in complete remission (CR). The sum of lesion length diameter decreased ≥30%, and was maintained at least 1 month for partial remission (PR). The total length and diameter of lesion decreased <30% or increases <30%. There were no new lesions found to be stable (SD), otherwise progress (PD). Effective = (CR+PR)/total number of cases x 100%.

Statistical analysis. The statistical analysis was performed by SPSS 20.0 software (IBM, Armonk, NY, USA). The measurement data were expressed as mean ± standard deviation. An independent sample t-test was used in the comparison between groups. The count data was expressed as a number of cases or (%). The comparison between groups was tested by χ^2. Survival was analyzed by the Kaplan-Meier model and log-rank χ^2 test. P<0.05 indicated that the difference was statistically significant.

Results

Comparison of therapeutic effects of two groups of metastatic lesions. The effective rate of the observation group was higher than that of the control group, and the difference was statistically significant (P<0.05) (Table I).

Comparison of complications. There were no differences in the incidence of complications between the two groups (P>0.05) (Table II).

Comparison of progression-free survival, median survival time and survival rate. The progression free survival, median survival time and survival rate of the observation group were increased; differences were statistically significant (P<0.05) (Table III).

Discussion

It has been found that the primary tumors with a diameter >2 cm can release ~3-4x10^6/g tumor cells per day into the blood circulation (7). Endothelial cells of the hepatic blood sinus lack the basement membrane and membrane, with 0.1 μm small holes. The liver blood volume is larger, the flow rate is slow and there is a lack of the necessary barriers to the transfer of cells. This causes the liver to be the place where bodies malignant tumors are easy to move (8). At the same time, cancer cells can stimulate the secretion of a variety of cytokines, including vascular endothelial growth factor, hepatocyte growth factor (9), and extracellular matrix components (10). This provides a powerful condition to the proliferation of the metastatic lesions.

Systemic chemotherapy is the standard treatment for breast cancer liver metastasis, but the liver of the drug uptake rate is up to >95%, with a significant first pass effect; the overall effective rate is only 30-55% (11). Due to poor general condition, multiple metastases, deep location, and closeness to the large blood vessels and so on, surgical resection is restricted (12). DSA hepatic artery angiography showed that most of the metastatic liver cancer showed a rich blood supply. Although most of the liver metastases transfer from portal vein, most of the blood supply is from the hepatic artery (13). TACE can increase the local concentration of chemotherapeutic drugs and reduce the side effects of systemic chemotherapy (14). They can combine iodine oil and gelatin sponge with an embolization of tumor blood vessels which control the slow release of chemotherapy drugs. Therefore, the tumor tissue will have hypoxia, necrosis and apoptosis (15). The median survival period will increase at least 5.0-8.0 months (16). As an important embolization agent, liquefied petroleum can be retained in the tumor tissue for a long time, a few months or even >1 year; the normal liver tissue can disappear after a few days. This feature is on the basis for the treatment of malignant liver tumors (17). TACE can significantly reduce the tumor size, and increase the chances of surgical resection (18). Good results can be achieved in patients with tumor thrombus in the portal vein or hepatic vein (19).

RFCA uses a high frequency electromagnetic wave ion shock to create heat, and therefore, the central temperature of the tumor reaches >60˚C. This causes the vascular occlusion and coagulation necrosis, resulting in killing of the tumor (20). Ultrasound guidance has advantages of real-time monitoring, accurate guidance, less trauma, safety and effectiveness, simple operation and repeatability (21). RFCA has a good application value in local liver cancer and renal cell carcinoma (22,23). The deficiency is that RFCA has the function of 'heat sink' and 'three dimensional leakage effect', which is not ideal in the tumors of large diameter and special locations (such as large blood vessel, diaphragm, gallbladder, heart and some other parts) (24). At the same time, the combination of RFCA and TACE can exert complementary advantages, and improve the effects of tumor treatment (25,26).

The results have shown that the effective rate of the observation group are higher than that of the control group. The progression-free survival and median survival time were prolonged, and the survival rate was improved. There were no differences in the incidence of complications. Results suggest that RFCA combined with TACE in the treatment of breast cancer with liver metastasis is safe and effective, and has good application value. Therefore, by increasing the sample size, extending the follow-up time, and controlling the influencing factors, these results can be further verified.

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