

Original Article

Elimination rate of tumor's blood supply, tumor necrosis rate and adverse reactions in advanced hepatocellular carcinoma treated by transcatheter arterial chemoembolization with radiofrequency ablation

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Abstract: Objective: To observe and compare the effects between transcatheter arterial chemoembolization (TACE) combined with radiofrequency ablation (RFA) and single TACE therapy on the elimination rate of tumor's blood supply, tumor necrosis rate and adverse reactions in patients with middle-advanced hepatocellular carcinoma (HCC). Methods: We selected 180 patients with middle-advanced HCC who were admitted in our hospital from January 2015 to March 2016. They were divided into TACE group (n=76) and TACE + RFA group (n=104) according to their treatment methods. The elimination rate of tumor's blood supply, total effective rate, tumor necrosis rate and incidence of adverse reactions were compared between the two groups. Results: The elimination rate of tumor's blood supply, total effective rate and tumor necrosis rate in TACE + RFA group were all higher than those in TACE group (P=0.003, P=0.000, P=0.002 respectively). The incidence of adverse reactions in TACE + RFA group was lower than that in TACE group (P=0.000). Conclusion: TACE combined with RFA can better block the blood supply to tumor focus, accelerate the tumor necrosis and reduce the incidence of adverse reactions of TACE.

Keywords: Transcatheter arterial chemoembolization, radiofrequency ablation, hepatocellular carcinoma

Introduction

There is no obvious symptom in occult early hepatocellular carcinoma (HCC), but once patients are found they suffer from HCC, most of whom have been in middle-advanced stage [1-3]. As an important treatment method for non-operative patients with middle-advanced HCC, the therapeutic effect of transcatheter arterial chemoembolization (TACE) is apparent; however, there exist some problems such as palindromia, poor long-term effect and liver function damage [4, 5]. Radiofrequency ablation (RFA) can release tumor antigen and enhance human body's immune responses to tumor, and thus plays a therapeutic role in HCC [6]. In clinical treatment for HCC, the application of TACE combined with RFA can effectively

improve the clinical therapeutic effect. In this study, 180 patients with middle-advanced HCC treated in our hospital from January 2015 to March 2016 were selected. The therapeutic effects and safety of the two groups were analyzed and reported as follows.

Materials and methods

General information

In this study, 180 patients diagnosed as middle-advanced HCC and treated in our hospital from January 2015 to March 2016 were selected. They were divided into TACE group (n=76) and TACE + RFA group (n=104) according to their treatment methods. This study has been endorsed by the Ethics Committee; all patients and their families signed informed consent.

Effects of TACE combined with RFA in advanced hepatocellular carcinoma

Table 1. Comparison of general information between two groups

Group	Age	Sex ratio (male/female)	Middle-advanced stage hepatocellular carcinoma	History of therapy (yes/no)	Child-Pugh class (A/B)
TACE group (n=76)	45.49±8.49	37/39	28/48	46/30	33/43
TACE + RFA group (n=104)	47.19±9.34	50/54	45/59	65/39	47/57
T/ χ^2	0.491	1.458	0.931	0.451	0.831
P value	0.194	0.096	0.151	0.311	0.093

Table 2. Comparison of the total effective rate between two groups (n, %)

Group	Cured	Markedly effective	Effective	Invalid	Total effective rate
TACE group (n=76)	49 (64.47)	11 (14.47)	9 (11.84)	7 (9.21)	60 (78.95)
TACE + RFA group (n=104)	71 (68.27)	21 (20.19)	7 (6.73)	5 (4.81)	92 (88.46)
χ^2 value					31.493
P value					0.000

Table 3. Comparison of the elimination of blood supply of tumor between two groups (n, %)

Group	Elimination of blood supply
TACE group (n=76)	45 (59.21)
TACE + RFA group (n=104)	89 (85.58)
T value	9.492
P value	0.003

Inclusion criteria: Patients with primary HCC who could not have operations or had unresectable tumors confirmed by clinicopathology and imaging, accorded with the guidelines for HCC treatment in *American Association for the Study of Liver Diseases* [7]; patients belonged to Child-Pugh class A or B; patients met the operation indications for TACE and RFA; patients had no tumor metastasis.

Exclusion criteria: Patients couldn't cooperate with the study; patients had other diseases; patients had the contraindications of TACE or RFA.

Therapeutic methods

TACE group: TACE was used in the TACE group (76 cases). Tumors were observed by CT images. When their number, location, volume and the peripheral blood supply were confirmed, TACE was performed. The right femoral artery was punctured. Embolization agent consisted of 50% of ultra-fluid lipiodol (GUERBET, France) and 45 mg of epirubicin (Nanjing Bangnuo Bio-

technology Co. Ltd.). The embolism was stopped until the lipiodol was completely deposited in the tumor focus.

TACE + RFA group: In addition to the use of TACE, the TACE + RFA group (104 cases) also adopted RFA, and punctured through the skin. American Radionics Cool-tip RF Ablation System (0-200 W, 480 kHz) was used, and it was performed through radiofrequency pulse transmission with cool-tip under local anesthesia. The ablation effect was evaluated by ultrasonography. If the tumor focus couldn't be clearly observed under ultrasound, the CT-guided approach was performed until there was no tumor focus.

Six weeks after the treatment, the observation indexes in two groups were observed and recorded.

Observation indexes

The tumorous condition was evaluated 6 weeks after the treatment in two groups. The assessment of tumor treatment efficacy was divided into "cured, markedly effective, effective and invalid". Cured: no tumor in the images and patients were proved to be cured by pathology; markedly effective: no tumor in the images; effective: the tumor become markedly small; invalid: there was no change in tumor focus. Total effective rate = cured rate + markedly effective rate. After the treatment, peripheral blood supply of tumor condition (the elimina-

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Table 4. Comparison of tumor necrosis rate between two groups (n, %)

Group	Total necrosis	Necrosis more than 50%	Necrosis less than 50%
TACE group (n=76)	42 (55.26)	17 (22.37)	17 (22.37)
TACE + RFA group (n=104)	69 (66.35)	28 (26.92)	7 (6.73)
χ^2 value		9.304	
P value		0.002	

Table 5. Comparison of adverse reactions between two groups

Group	Response of digestive tract	Skin response	Infection	Total incidence rate
TACE group (n=76)	5 (6.58)	4 (5.26)	1 (1.32)	10 (13.16)
TACE + RFA group (n=104)	4 (3.85)	2 (1.92)	1 (0.96)	7 (6.73)
χ^2 value	8.989	7.911	12.981	8.761
P value	0.008	0.004	0.000	0.000

tion rate of blood supply around the tumor was observed through angiography) and tumor necrosis condition (no tumor focus could be found by CT) in two groups were analyzed, so as to evaluate the treatment effect. The adverse reactions such as vomiting, pruritus and infection in two groups were recorded and counted during the treatment.

Statistical methods

SPSS13.0 software was used for statistical analysis. The measurement data was expressed as mean \pm standard deviation and tested by two independent samples t-test. Enumeration data was expressed as rate or percentage, and tested by chi-square test. $P < 0.05$ meant the difference was statistically significant.

Results

Comparison of the general information between two groups

The general information between two groups was not statistically different and it was comparable. See **Table 1**.

Comparison of the therapeutic effect between two groups

The proportion of cured and markedly effective in TACE + RFA group was better than that in TACE group. The total effective rate in TACE +

RFA group (88.46%) was higher than that in TACE group (78.95%) ($P < 0.05$). All details were shown in **Table 2**.

Comparison of the elimination of tumor's blood supply between two groups

As shown in **Table 3**, the elimination rate of tumor's blood supply in TACE + RFA group (85.58%) was significantly higher than that in TACE group (59.21%) ($P < 0.05$).

Comparison of tumor necrosis condition between two groups

The tumor necrosis condition in TACE + RFA group was better than that in TACE group ($P < 0.05$). All details were shown in **Table 4**.

Comparison of adverse reactions between two groups

The complication rates in TACE + RFA group were lower than those in TACE group, and the total incidence rate (6.73%) was lower than that in TACE group (13.16%) ($P < 0.05$). All details were shown in **Table 5**.

Discussion

TACE plays an anti-tumor effect by cutting off the tumor's blood supply. Because tumors mainly rely on the human blood to absorb nutrition, once their nutrition source is cut off, their growth will be restrained [8]. In TACE, chemotherapy drugs and embolic agents are infused into the arterial blood supply of HCC, and then chemotherapy drugs were slowly released and retained in the blood vessels, which can have a long-term effect and thus effectively inhibit the growth of tumor cells [9-10]. RFA belongs to an interventional therapy in clinic, which has been widely used in cancer treatment. Clinical studies have shown that the effect of RFA is generally the same as surgical effect [11, 12]. RFA converts all kinds of energy into heat energy; in this process, the environmental temperature of tumor cells rises continuously, when it is up to a certain extent, structures and internal proteins of tumor cells will be destroyed to varying

degrees, thereby to induce tumor cell apoptosis and destroy tumor cells [13, 14].

The results in this study showed that the therapeutic effect of TACE combined with RFA was significantly improved, and the blood supply of tumor was decreased. It illustrated that RFA had a certain killing effect on blood vessels that support tumor growth, and was able to effectively improve the curative effect of chemotherapy drugs in blood vessels and block the nutrients and energy sources for tumor growth, thereby inhibiting the regrowth of tumor cells [15, 16]. TACE therapy used in the TACE + RFA group mainly kept tumor cells from growing and made them gradually atrophy and die in the absence of nutrients, but after combined with RFA, it directly acted on tumor cells and had direct killing effects [17, 18]. Perez, et al. treated cancer patients with embolization and ablation, whose results were consistent with the results in this study [19]. Yagi et al. found that the incidence of adverse reactions in TACE + RFA group was significantly higher than that in TACE group, which may be because these two treatment methods both had adverse reactions; there were few coincident adverse reactions in one patient in Yagi's study, but some in this study [19, 20]. A few coincident adverse reactions suggest the small sample size in this study, so we need to increase the sample size in the future study, and statistically analyze the incidence of adverse reaction according to its frequency, thus to obtain more accurate statistical data.

In summary, TACE combined with RFA treatment can improve the tumor necrosis rate. TACE combined with CT-guided RFA for primary HCC is a safe therapeutic method and has simple practical operation, which can effectively control the local regeneration of tumor and prolong the survival time of patients.

Disclosure of conflict of interest

None.

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