

ORIGINAL ARTICLE

## Transcatheter arterial chemoembolization combined with microwave coagulation therapy and the perioperative care for patients with hepatocellular carcinoma

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### Summary

**Purpose:** To explore the value of artificial hydrothorax microwave coagulation combined with transcatheter arterial chemoembolization (TACE) therapy in the treatment of ultrasound-invisible malignant tumors in the hepatic dome (mainly hepatocellular carcinoma/HCC) and the perioperative care for the patients.

**Methods:** Sixty-eight patients with malignant liver tumors in the hepatic dome were treated with a combination therapy of TACE and microwave coagulation via an artificially induced hydrothorax. Their perioperative condition was under close observation and the nursing care was intensified. Paracentesis of the chest was successfully carried out via the positioning of ultrasound and guidance of microwave to the tumor site, so that the tumor could be treated with cold cycle microwave coagulation therapy.

**Results:** After treatment, 3/68 patients (4.4%) achieved complete tumor ablation, while 59/68 (86.8%) achieved tumor ablation >50% or tumor shrinkage >30%. Another 6/68 patients (8.8%) achieved tumor ablation <50% or tu-

mor shrinkage <30%. Of 45 patients, 42 (93.3%) obtained a reduction of AFP level >50% post-therapy, 28/37 patients (75.7%) achieved a reduction of CEA level >50%, 23/29 patients (79.3%) achieved a reduction of CA19-9 level >50%; 3/68 patients (4.4%) survived for 4 to 6 months, 31/68 (45.6%) survived >6 months and 34/68 (50%) survived >12 months. No bleeding, liver failure, infection or needle tract seeding occurred after the operation, and no treatment-related deaths occurred.

**Conclusion:** Microwave coagulation combined with TACE for HCC in the hepatic dome is safe and effective. Perioperative observation and nursing care can not only reduce the complications but also improve the therapeutic effect and the patient quality of life.

**Key words:** hepatocellular carcinoma, microwave coagulation therapy, postoperative care, transcatheter arterial chemoembolization

### Introduction

According to the annual data of 2011, there are more than 695,000 people dying from primary HCC each year worldwide [1], among which there are about 120-140,000 patients from China. Surgery is one of the main treatments for primary HCC, but less than 30% of the patients are suitable for surgery [2]. In the non-surgical treatments for HCC, TACE is the preferred method. However, due to the uneven and double blood supplies in

tumor tissue, interventional therapy alone can not produce satisfactory results for HCC [3]. B ultrasound-guided percutaneous microwave coagulation therapy (PMCT) is a new technology for cancer treatment. In particular, the ultrasound-guided microwave ablation (MWA) has been proven to be one of the safe and effective ways in the treatment of HCC [4-7]. Ablation therapy for early HCC can obtain almost similar long-term survival com-

pared with surgical therapy [8]. However, due to the gas inside the lung tissue, tumor in the hepatic dome can hardly be detected by ultrasound [9]. CT-guided detection is not influenced by the lung tissue, but CT-guided percutaneous puncture and treatment are easy to hurt the lung tissue and may lead to various complications, such as pneumothorax, hemothorax, biliary tracheal fistula and so on [10]. Artificial hydrothorax can put aside the gas-containing lung tissue and form a good ultrasonic medium within the costophrenic angle, so that the lesions in the hepatic dome can be detected by ultrasound and facilitate the regional treatment [11,12]. Furthermore, keeping the patients under observation and intense nursing care during the perioperative period is essential for smooth patients' recovery.

In the present study we retrospectively analyzed 68 patients with HCC in the hepatic dome, who were hospitalized and received interventional therapy combined with artificial hydrothorax microwave coagulation therapy from 2001 to 2008.

## Methods

### *Clinical data*

Sixty-eight patients (39 male and 29 female) with HCC in the hepatic dome, were enrolled in this study. There were 46 cases of primary HCC and 22 cases of metastatic hepatic carcinoma (lung cancer 8 cases, breast cancer 5, gastric cancer 6 and colon cancer 3 cases). In 47 patients the maximum tumor diameter ranged from 5 to 10 cm and in 21 cases the maximum tumor diameter was > 10 cm. The Child-Pough classification of the liver function was grade A and B and the Karnofsky performance status scores were all higher than 50. This study was conducted in accordance with the declaration of Helsinki and after approval from the Ethics Committee of Liaocheng People's Hospital. Written informed consent was obtained from all participants.

### *TACE treatment*

TACE was carried out using Seldinger technology. In brief, a 517/4 F catheter was inserted percutaneously into the celiac artery/superior mesenteric artery through the femoral artery. Then, angiography was performed using high pressure injector to determine the location, size and blood supply of the tumor. As the blood vessels that supplied the tumor were super-selected, chemotherapeutic drugs (FUdR 1.0 g, cisplatin 60-80 mg, mitomycin-C 10-20 mg or epirubicin 80 mg and 5-30 ml iodized oil were injected into the tumor. Sometimes, gelatin sponge was also needed for certain patients to strengthen the embolization of blood vessel in tumor.

### *Preparation of artificial hydrothorax*

Patients were asked to keep in semi-recumbent position to perform the ultrasound pre-scan firstly. The bottom of the lung was explored by ultrasound along the right mid-axillary line and then the position of the needle insertion was determined. Thoracentesis was performed using central venous puncture needle that was connected to an infusion apparatus. As the needle entered the subcutaneous tissue, the control switch of the infusion apparatus was opened. Then the needle was inserted continually and slowly until there were droplets of normal saline dripped fast into the bucket which changed with respiration. Then the needle was successfully inserted into the thoracic cavity. Subsequently, the switch of the infusion apparatus was closed and a central venous catheter was inserted via the needle and fixed on the skin. In order to prevent infection, the puncture site was bandaged. Under ultrasound guidance, 1-2 liters of normal saline were infused into the thoracic cavity in full speed via the central venous catheter until the lower pole of the lung was pushed aside to expose the puncture pathway for the intrahepatic lesions. As the PMCT finished the normal saline in the thoracic cavity was drained out via the central venous catheter. The catheter was left in place for 2-3 days for the next treatment.

### *Percutaneous microwave coagulation therapy (PMCT)*

LOGIC-5 ultrasonic apparatus (GE, Conn. Fairfield City, USA) was used for confirming the presence of hydrothorax, and METI-IVB microwave therapeutic apparatus (Nanjing Institute of New Technology Co., Ltd., Nanjing, China) was used for the microwave ablation. The full procedure of PMCT was performed under sterile conditions. As the artificial hydrothorax was established and the patients were anesthetized, a 14 G needle was inserted into the tumor through the chest and diaphragm with the guidance of ultrasound. Then the needle core was pulled out and the microwave antenna was subsequently inserted into the guide needle until it reached the tip of the needle. After that, the guide needle was slowly withdrawn until the anterior extremity of the microwave antenna was exposed about 2.7 cm. Microwave coagulation was then performed with the time and power determined by the tumor size and the distribution of the blood vessels with tumor diameter <3.0 cm, 80 W of microwave energy for 600 sec could achieve overall tumor coverage and kill effectively the tumor cells. However, if the tumor size was >5.0 cm, a combinatorial way with multi-pin, multi-point and multi-faceted was needed. The distance between the two pins should be  $\leq 15$  cm and the therapy should last for 10-15 min. If the tumor diameter was between 3 and 5 cm, one-pin or two-pin joint treatment should be used, depending on the treatment conditions. The microwave coagulation therapy should cover the whole edge of the tumor. Meanwhile, ice packs were used to protect the skin from scorch. Before finishing the

**Table 1.** Degree of tumor ablation

Degree of tumor ablation	Complete tumor ablation	Ablation >50% or tumor shrinkage >30%	Ablation ≤50% or the tumor shrinkage ≤30%	Total
Number	3	59	6	68
%	4.4	86.8	8.8	100

PMCT, the microwave antennas were withdrawn a bit into the place between the surface of the liver capsule and the chest walls and then the additional microwave coagulation was performed for 5-10 sec to stop bleeding and prevent tumor seeding along the needle track.

#### Perioperative care

According to the physician's instructions, the routine examinations for the patients were improved. The patients were asked to fast for 4-6 hrs and evacuate pre-procedure.

#### Postoperative care

Post-procedure, the patients were nursed in a routine way. They should have an absolute bedrest for 12 hrs in supine position. Electrocardiographic monitoring lasted for 24 hrs and the blood pressure, pulse, consciousness, language expression and bleeding at the puncture site were also under close observation. The puncture site was treated with conventional regional pressure dressing to stop bleeding. If regional bleeding occurred, dressings should be changed promptly. If the patients complained of increased pain at the surgical site, liver bleeding should be considered and notified to the physician promptly.

Because of the anesthetics and analgesics, some patients developed nausea, vomiting and other gastrointestinal symptoms intraoperatively or postoperatively. Good psychological care was particularly important to relieve the psychological burden. If necessary, the symptoms should be notified to the physician and treated in time.

#### Diet care

Patients could eat normally after the procedure since the local anesthesia during the microwave and TACE therapies did not cause obvious discomfort. However, only light diet was allowed.

#### Fever care

Patients developed postoperative fever of various degrees, which mostly occurred at the absorption period. Most patients developed fever >38°C or even 38.6°C. This was caused by absorption fever and the patient was informed about this beforehand. Appropriate anti-

pyretics and antibiotics were used intravenously until the body temperature returned to normal.

#### Efficacy evaluation

One month after treatment, patients were re-checked clinically, with CT scanning, B ultrasound and assessment of liver function, AFP, CEA and CA 19-9. The lipiodol deposition, tissue ablation dimension and tumor shrinkage were observed and assessed. If the tumors were completely ablated, the CT scanning showed no enhanced low density regions and B ultrasound showed high-level echo without any blood flow.

## Results

#### Therapeutic efficacy

After receiving TACE combined with PMCT, 3/68 patients (4.4%) achieved complete tumor ablation, 59/68 patients (86.8%) achieved tumor ablation >50% or tumor shrinkage >30%. Another 6/68 patients (8.8%) achieved tumor ablation <50% or tumor shrinkage <30% (Table 1). Among 45 cases with preoperatively increased AFP level, 42 (93.3%) obtained a reduction of AFP level >50% post-therapy. Among of 37 cases with increased serum CEA level pre-therapy, 28 (75.7%) cases achieved a reduction of CEA level >50%. For the 29 cases with preoperatively elevated serum CA19-9 level, 23 (79.3%) achieved a reduction of this marker level >50% (Table 2). Three patients (4.4%) survived for 4 to 6 months, 31 (45.6%) survived >6 months and 34 (50%) survived >12 months, among which there were 2 cases still alive without recurrence (Table 3).

#### Adverse reactions and complications

Following treatment with TACE, the major adverse reactions of the patients were gastrointestinal symptoms, chemotherapy-induced leucopenia and liver dysfunction. The major adverse reaction for PMCT was hepatalgia, especially pain in the tumor site near the liver capsule. Fortunately, it

**Table 2.** Change of tumor markers

	<i>Preoperatively elevated</i>	<i>Postoperatively declined by &gt;50%</i>	<i>%</i>
AFP	45	42	93.3
CEA	37	28	75.7
CA199	29	23	79.3

**Table 3.** Patient survival after treatment

	<i>4-6 months</i>	<i>6-12 months</i>	<i>&gt;12 months</i>	<i>&gt;24 months</i>	<i>Total</i>
Number	3	31	34	2	68
%	4.4	45.6	50	2.9	100

could be relieved after symptomatic treatment. No bleeding, liver failure, infection or needle tract seeding occurred after the operation, and no treatment-related deaths occurred.

## Discussion

The combination therapy of TACE and PMCT used for advanced HCC follows the principles of combined therapies and mutual complement of advantages [13]. Most patients with advanced HCC are not sensitive to chemotherapy and radiotherapy, which could offer only short survival benefit to a limited number of patients. TACE and PMCT combination has a synergistic therapeutic effect that is more efficacious than single treatment method alone [14]. TACE is the preferred treatment for unresectable bulky HCC, but it has rather poor therapeutic efficacy if used alone [3]. The reasons may be as follows: firstly, the tumor blood supply is asymmetric, which leads to incomplete embolization; secondly, there are arteriovenous communications between the hepatic artery and portal vein or the hepatic artery and hepatic vein, leading to quick loss of the drug in the tumor tissue, which makes the method not suitable for embolism; thirdly, there is less blood supply in some tumors, leading to poor embolic results.

The main obstacle for the microwave ablation is the heat-sink effect. That is, during the ablation process, the heat is constantly taken away by the peripheral large blood vessels, which could affect the heat accumulation. Due to the fast atten-

uation of the central temperature of microwave, PMCT is mainly used for the treatment of small HCC with diameter <3cm. Complete ablation of small HCC can reach 80% or even 90% and its local recurrence rate is 5-15% [12]. In this study, we expanded the application range of microwave tissue coagulation, so that more patients with advanced liver cancer could benefit from treatment. However, regional treatment will lead to tumor vascular occlusion, which is not facilitated from the lipiodol deposition and chemotherapy drugs entering into the lesion during the TACE. Thus, we carried out TACE treatment first, to avoid the aforementioned problems. TACE is based on the lipiodol embolization in the tumor blood vessels to reduce the blood flow, which can suppress the heat loss of the subsequent PMCT and increase its therapeutic efficacy. After PMCT, TACE was performed one more time. Microwave coagulation is able to close some arteriovenous communications and extend the time of lipiodol deposition in residual lesions [13].

In the past, ultrasound could hardly show liver tumors located just below the diaphragm, because of the interference of the pulmonary gas, making thus the percutaneous microwave therapy difficult to carry out. Even though the lesions may be partly exposed, the treatment can not destroy tumor cells completely because the therapist tries to avoid any damage in the lung and diaphragm. With the use of artificial hydrothorax, microwave coagulation therapy for HCC located at the top of the liver can

not only help ultrasound to show the tumor more clearly but also to reduce the incidence of complications [15,16]. Artificial hydrothorax is a feasible, safe and effective method, which further expands the application range of ultrasound-guided microwave treatment. With our methodology we achieved an improvement of the procedure. Briefly, we punctured with a fine needle first, which is safer and easier to be inserted into the thoracic cavity with the guidance of ultrasound. Secondly, a deep venous

catheter was inserted via the needle catheter to accelerate the formation of pleural effusion. Meanwhile, this could be used to drain out the pleural effusion postoperatively, helping thus to observe the postoperative complications and to reduce the patient's chest tightness and other symptoms of oppression. In addition, if a second microwave treatment is needed, the venous catheter can also be used directly to produce artificial pleural effusion and thereby reducing the pain and costs of the procedure [17,18].

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