



Journal of Health and Medical Sciences

Fiaz, Muhammad, Malik, Ammara Saeed, and Ramzan, Muhammad. (2020), Combination Therapy with TACE and Microwave Ablation to Increase Efficacy of Hepatocellular Carcinoma Treatment. In: *Journal of Health and Medical Sciences*, Vol.3, No.1, 98-103.

ISSN 2622-7258

DOI: 10.31014/aior.1994.03.01.103

The online version of this article can be found at:
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Published by:
The Asian Institute of Research

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Combination Therapy with TACE and Microwave Ablation to Increase Efficacy of Hepatocellular Carcinoma Treatment

Muhammad Fiaz¹, Ammara Saeed Malik², Muhammad Ramazan³

^{1,2,3} Superior University Azra Naheed Medical College and Alrazi Hospital, Lahore, Pakistan

Abstract

To evaluate efficacy of microwave ablation (MWA) combined with conventional transarterial chemoembolization (cTACE) simultaneously or vice versa for the treatment of large hepatocellular carcinoma (HCC). Study was done from March 2017 and February 2019 and a total number of 66 patients with large hepatocellular carcinoma received TACE and ultrasound-guided percutaneous MWA combined with simultaneous TACE. Patients with primary liver cancer aged from 18-80 years, and life expectancy longer than three months were included. Ablation with different techniques were used along with standard doxorubicin TACE. As result, it was concluded that the combined treatment model is superior to single TACE.

Keywords: Hepatocellular Carcinoma, Microwave Ablation, Transarterial Chemoembolization

Purpose

To validate the efficacy of microwave ablation (MWA) combined with conventional transarterial chemoembolization (cTACE) simultaneously or vice versa for the treatment of large hepatocellular carcinoma (HCC).

MATERIALS AND METHODS

- From March 2017 and February 2019, a total number of 66 patients with large hepatocellular carcinoma received TACE (N=33) or ultrasound-guided percutaneous MWA combined with simultaneous TACE (N=32). One case was deferred.
- This prospective selected study was discussed in detail and approved by our hospital Ethics Committee.
- This specific treatment procedure of combination therapy was done on digital subtraction angiography (DSA) for TACE, followed percutaneous MWA (Microwave ablation) under ultrasound But in some cases we reversed the pattern with MWA first followed by TACE.,

1. Imaging examinations:

Multiphasic CT or Multiphasic MRI imaging

2. laboratory tests:

Alpha-fetoprotein (AFP) levels (which were conducted after 6-8 weeks following procedure and every 8-12 weeks thereafter)

3. According to the modified Response Evaluation Criteria in Solid Tumors (m-RECIST), The tumor response:

- (1) Complete Response (CR)
- (2) Partial Response (PR)
- (3)Stable Disease (SD)
- (4)Progressive Disease (PD)

Local residual or recurrence is defined as the presence of enhancement within or around the treated area of the tumors after 1 month of treatment.

- **Repeat MWA-TACE or serial TACE was considered based on the hepatic function, post procedure status and patient's performance status.**
- **Assessment and comparison was made for local tumor response, progression-free survival (PFS) and overall survival (OS).**
- **Statistical analysis: Kaplan-Meier method, independent *t*-tests and chi-squared.**

INCLUSION CRITERIA

1. Patients with primary liver cancer aged from 18-80 years, and life expectancy longer than three months;
2. Large HCC (>5cm in diameter) and huge HCC (>=8cm in diameter),
3. Portal vein must be thrombus free.
4. LFTs classified as Child-Pugh A or B, ECOG PS ≤ 2 ;
5. No abnormal bleeding tendency
6. White blood cell count atleast $\geq 3.0 \times 10^9/L$;
7. Hemoglobin ≥ 9 g/dl;
8. Platelet $\geq 100 \times 10^9/L$;
9. INR ≤ 1.8 or PT not exceeding the upper limit of reference 3 seconds;
10. Blood creatinine must be less than 1.5 times of upper limit of reference;
11. Informed consent was done for Patients and/or their relatives willing to join in this clinical trial.

EXCLUSION CRITERIA

1. Diffuse type of liver cancer;
2. Thrombus in main portal vein (PV)
3. Hepatic vein thrombus;
4. Lymph node or distant metastasis outside of liver;
5. Liver function classified as Child-Pugh C
6. Coagulation disorder and abnormality
7. Intractable massive ascites;
8. ECOG PS > 2 ;
9. Active infection, especially cholangitis;
10. Severe disorders of heart, lungs, kidneys, or brain;

THE TREATMENT PROCEDURES

1. TACE combined with ablation or MWA combined with TACE synchronously group

- (1) Hepatic DSA (arteriography) is performed to investigate the tumor's location, size, number and to evaluate feeding artery and any shunt.
- (2) MWA is performed under ultra-sound guidance. General anesthesia is done.

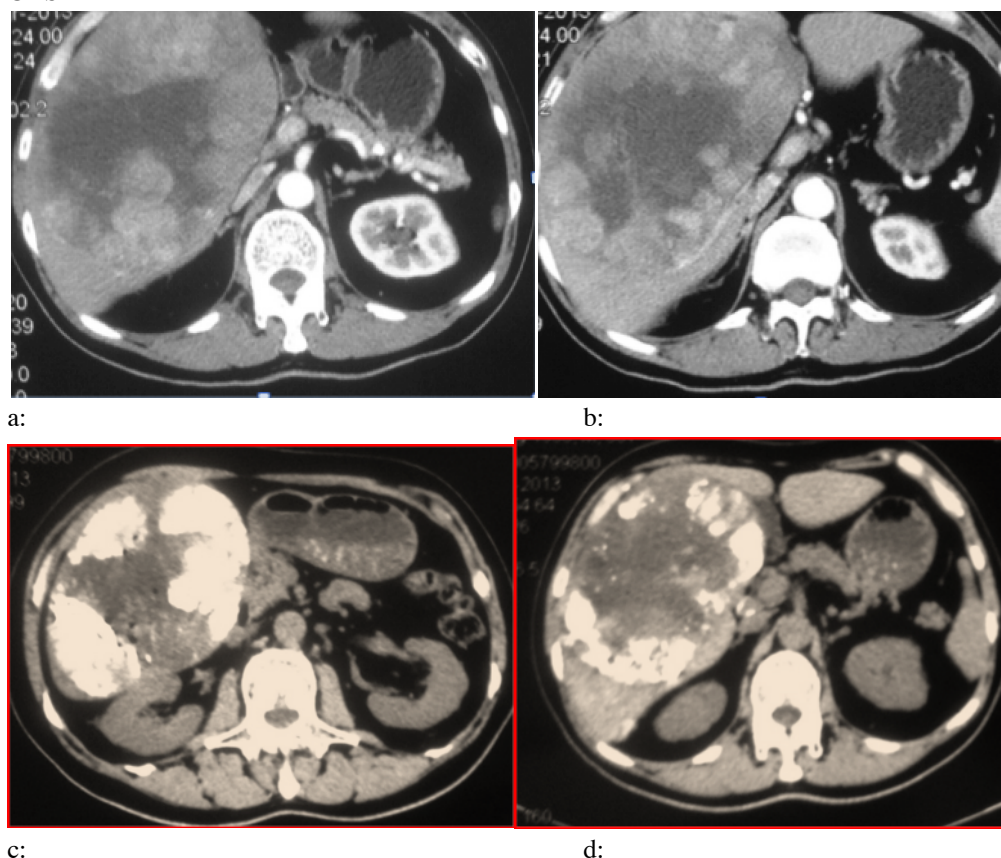
- ◆ The ablation technique with three electrode needles (switching needles) placed at multiple different points were usually performed.
- ◆ Extent of ablation zone must reach or exceed more than two-thirds size of target tumors.
- ◆ TACE were immediately performed after MWA finished or similarly MWA were performed after completion of TACE procedure.

TACE PROCEDURE

Chemotherapy drug: Doxorubicin 30-50mg;

- ◆ Lipiodol Ultra-Fluide (Guerbet, France): < 20ml
- ◆ Embolization material: gelatin sponge articles with 350-560um in diameter will be used.
- ◆ We put catheter in celiac axis followed by micro catheter at the feeding artery branch of the tumor and inject the emulsion of 20-30mg of Doxorubicin and 5-10ml of ultra-fluid lipiodol , and then followed the particulate embolic agent (such as gel foam)

CASE 1



Case 1: Large HCC in right lobe of liver. Fig a and b are showing post ablational scan with a large ablated area. Fig c and d are showing scan followed by TACE.

RESULTS

Objective response rate:	
(1) MWA-TACE group or TACE-MWA group	(2) In TACE group Only
CR : 32.5% (21/ 65)	CR : 10.9% (7 / 66)
PR : 47.1% (31/65)	PR : 31.8% (21/66)

CR+PR : 80.6%.	CR+PR : 48.0%

Objective response rate was better in MWA-TACE group than in TACE group ($P=0.001$).

Overall and progression-free survival	
(1) The median survival time:	MWA-TACE group: 14 months . TACE group: 9 months
(2) The 6-, 12- and 18-month OS rates	MWA-TACE group: 80.5%, 35.9%, 50.6% TACE group: 65.5%, 40.2%, 20.3%
(3) The 6-, 12- and 18-month PFS rates	Which were 60.9%, 25.1%, 16.9% and 37.4%, 6.2%, 3.7% in MWA-TACE group and TACE group respectively.
(4) The median PFS time	MWA-TACE group: 9 months TACE group: 4 months

◆ **The difference was significant between the two groups ($P<0.05$)**

3. AFP and hepatic function:

- AFP values before treatment

MWA-TACE group: 14175.0ng/ml $\pm$ 23241.1ng/ml,

TACE group : 13873.7ng/ml $\pm$ 21652.2ng/ml

AFP values one month after treatment

MWA-TACE group: 4218.4ng/ml $\pm$ 13716.1ng/ml

($P<0.001$)

TACE group : 7107.2ng/ml $\pm$ 15485.8ng/ml

($P<0.001$)

◆ **The difference was significant** between the two groups after treatment ($P<0.001$). The decrease of AFP in the MWA-TACE group was higher than the TACE group.

THE LIVER FUNCTIONS

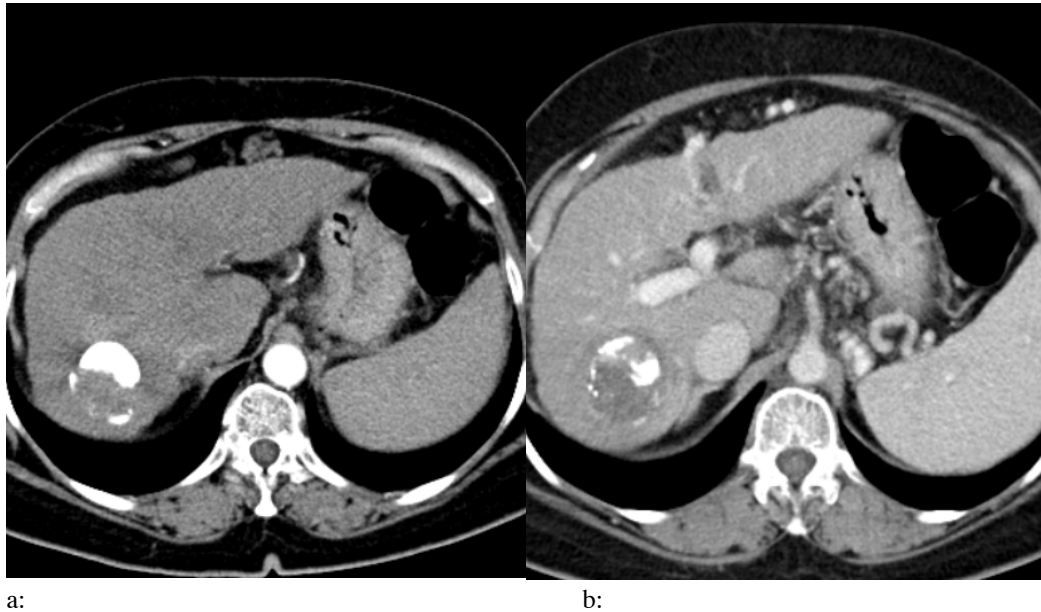
- The liver function was improved in MWA-TACE and TACE group after treatment, the difference was significant between the two groups ($P<0.05$).

4. Side effect

- Post-embolization syndrome : including mild-to-moderate pain, fever, nausea and vomiting
- A hemorrhage:
MWA-TACE group: 3 patients (treated by TAE)
- A liver abscess
TACE group: 3 patients (treated with tube drainage) (detected 1 month after treatment)

◆ **The combination therapy was well-tolerated in all patients, and no major complications or procedure-related mortalities were observed.**

CASE 2



Case 2: CT images after ablation and TACE.

Objective response rate was better in MWA-TACE group than in TACE group ($P=0.001$).

◆**The difference was significant between the two groups . ($P<0.05$)**

Conclusion

- According to our results, MWA combined with simultaneous TACE therapy or TACE combined with MWA therapy can be performed safely and effectively in patients with large or huge HCC
- There were NO major complications.
- The combined treatment model is superior to single TACE. It enlarged the indications of mult needle MWA in large HCC, and was worth to be promoted.

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