

Research article

Effect of combination between Trans catheter arterial chemoembolization followed by Radiofrequency ablation to optimize the treatment outcome in management of large sized HCC

Hosny S. A. Ghany, Mohmed A. Shweel, Mohmed A. Ibrahiem, Mostafa M. Elian and Mohmed F. Rohiem

Department of Radiology, El Minia University Hospital, Minia Faculty of Medicine, Egypt

Abstract

Purpose: to access the efficacy of combination therapy between TACE and RF ablation in treatment of large sized solitary hepatocellular carcinoma (3-7cm diameter) or associated with other satellites of tumor fosse in terms of improving the patient's survival and quality of live.

Materials and methods: A prospective study carried in 40 patients who underwent TACE followed or preceded by RF ablation in sequential or actual combination manner with follow up of the treatment outcome was done through Triphasic CT study and lab data of liver function tests and AFP at 1,3,6,9 and 12 months. **Results:** for TACE followed by immediate RFA, complete response 60%, partial response in 10% and 20% developed disease progression detected at 9&12 months follow up. For RFA followed by immediate TACE, complete response 0%, partial response in 20% and 30% developed disease progression detected at 9&12 months follow up. For sequential TACE post previous RFA, complete response 0%, partial response in 20% and 30% developed disease progression detected at 9&12 months follow up. For sequential RFA post previous TACE, complete response 20%, partial response in 20%, stable disease in 10% and 30% developed disease progression detected at 6,9 and 12 months follow up. **Conclusion:** Actual combination modality of TACE followed by RFA is a treatment modality of choice that could be employed in different problematic HCC situations as lesions of size range 3-7cm diameter, morphology of ill defined tumor margins) or associated with small satellites in its vicinity.

Keywords: Hepatocellular carcinoma (HCC), RF ablation (RFA) and Tran's arterial chemoembolization (TACE).

Introduction

Hepatocellular carcinoma (HCC) is a challenging malignancy in terms of management and its complex etiology. For most patients with HCC, unfortunately curative treatment is limited due to the underlying liver dysfunction mostly resulting from liver cirrhosis and only 10-30% are surgical candidate for liver resection or liver transplant.⁽¹⁾ performed principally in patients with small HCC (≤ 3 cm in diameter). In recent years, the use of RFA has also been considered for the treatment of medium sized HCC (3-7 cm).⁽²⁾

Performing TACE prior to RFA is beneficial in that it achieves better ablation than either TACE alone or RFA alone in

selected candidates with hepatocellular carcinoma greater than 3 cm. This result could be explained by the modification in hepatocellular carcinoma tissue conduction that occurs after the sudden hemodynamic changes caused by occlusion of the hepatocellular carcinoma feeding artery.⁽³⁾

Patients and Methods

The study included 40 patients and carried out at Radiology Department, Minia university hospital, Minia, Egypt, from April 2011 to February 2016.

Inclusion Criteria:

- HCC Confirmed by both MDCT and alpha fetoprotein level.
- Unresectable tumor.
- Good baseline liver dysfunction.

- Patient general status and tumor stage.

Exclusion Criteria:

- Patients with decompensated liver including Child-Pugh class C and Okuda stage of Grade III.
- Main portal vein obstruction.
- Serum creatinine concentration of ≥ 1.36 mg/dL.

Interventional Procedures used in the study

A- TACE: Celiac arteriography, selective hepatic angiography and superior mesenteric arteriography to determine the vascular anatomy, portal blood flow, to identify the feeding

RF ablation post TACE sequential combination group:

Twenty patients included in sequential RF ablation post TACE group with the patients previously underwent TACE and during their follow up, some patients developed either local/ marginal recurrence or newly developed lesion at different hepatic segment with the lesion were in the size criteria of RF ablation. The selection of the most appropriate treatment option for HCC patients depends not only on their patients included in RF ablation

Radiofrequency ablation (RFA) has been arteries and the presence of intra tumor arterio-venous shunting.

B- RF ablation; A (RITA), 10-gauge insulated RFA electrode with 9 expandable electrode tines that cover a range 2-6 cm in diameter at expansion used in the study (RITA 1000X RF generator and RITA Star Burst Xli enhanced electrode, RITA Medical Systems, Mountain View, California).

Results

The study included 70 patients with mean patient's age 53.3 ± 11.7 (range 43-67

years), 46 patients (67.1%) were males and 24 patients (34.2%) were females. All patients had HCC on top of cirrhotic liver and among risk etiological factors; positive hepatitis C was dominant in (64.2%), Hepatitis B positive in (31.4%), combined positive B and C in (2.8%) and (1.4%) was alcoholic addict. The selected group of patients included in the study divided into 4 subgroups based on patient end point at time of follow up (previous treatment), tumor size, number, location, morphology, and overall patient clinical performance.

TACE followed by RF ablation actual combination group:

Twenty patients included in the TACE followed by RF ablation actual combination group with patients pre planned from the start for combined TACE followed by RF ablation within two weeks as their tumor size was in the size range 3-7cm diameter, morphology (ill defined tumor margins) or associated with small satellites in its vicinity.

RF ablation followed by TACE actual combination group:

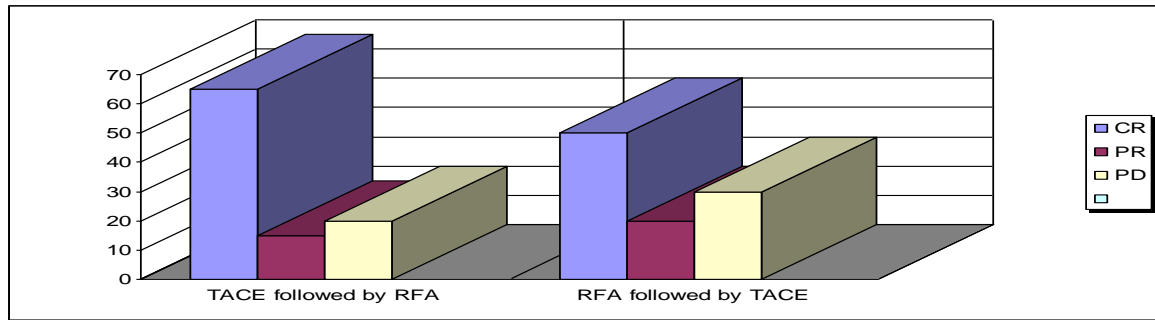
Twenty patients included in RF ablation followed by TACE in the actual combination group, for this group tumor size range was (3-6 cm diameter), but the margins were ill defined far microscopic extension or satellites.

TACE post RF ablation sequential combination group:

Twenty patients included in sequential TACE post RF group with the patients previously underwent RF ablation and after long period of follow up, these patients developed either multiple recurrent lesions or large marginal/ infiltrative local recurrence.

Table (1): Treatment outcome for actual combination therapy groups after one year follow up.

Treatment outcome	TACE followed by RFA		RFA followed by TACE	
	N(20)	%	N(10)	%
Complete response	13	65%	0	0.0%
Partial response	3	15%	2	20.0%
Progressive disease	4	20%	3	30.0%



Graph (1): Treatment outcome for actual combination therapy groups after one year follow up.

Table (2): Comparison between procedures related complications for actual combination therapy groups

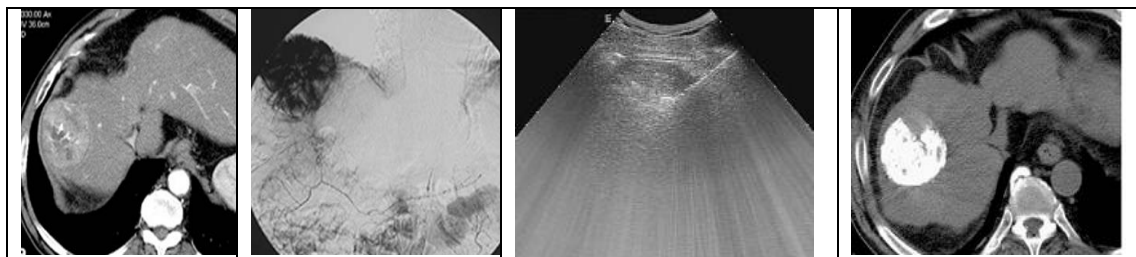
Complications	TACE followed by RFA		RFA followed by TACE	
	N(20)	%	N(10)	%
Post embolization syndrome	13	65%	8	80%
Reversible Liver cell impairment	3	15%	3	30%
Overt liver cell failure	-	-	-	-
Portal vein thrombosis	1	5%		
Infectious focus	-	-		

Table (3): Treatment outcome for sequential RF post TACE after one year follow up.

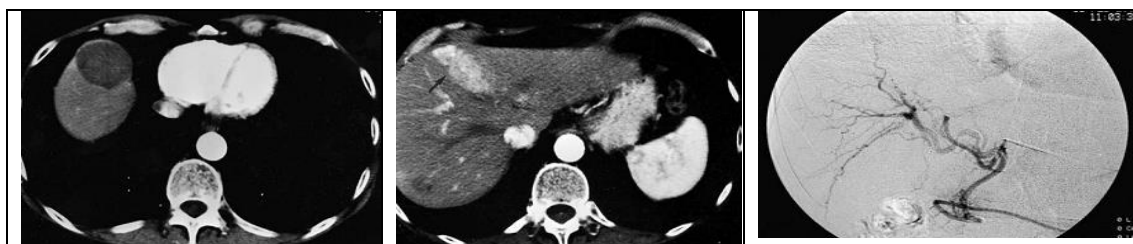
Treatment outcome	N	(%)	Timing(months)
Complete response (CR)	10	50 %	12 months
Partial response (PR)	4	20 %	3 months
Progressive disease (PD)	6	30 %	9&12 months

Table (4): Treatment outcome for sequential TACE post RFA after one year follow up.

Treatment outcome	N	(%)	Timing(months)
Complete response (CR)	4	20 %	12 months
Partial response (PR)	0	20 %	3 months
Progressive disease (PD)	9	45 %	6&9&12 months
Stable disease (SD)	2	10 %	3 months



Case (1): TACE followed by RFA actual combination with partial response.



Case (7): RFA followed by TACE actual combination with devascularisation.

Discussion

Performing TACE prior to RFA has theoretical merits: first; occlusion of hepatic arterial flow by means of embolization may contribute to the decrease in the heat-sink effects during RFA and increase the ablation volume by RFA⁽¹¹³⁾. Second; combined treatment may have the effect of anticancer agents on cancer cells, which is enhanced by the hyperthermia.

Radiological follow up of the treatment outcome through Triphasic CT scans at 1st, 3rd, 6th, 9th months and by the end of one year revealed that the treatment response were complete in 70%, partial in 10% and 20% suffered from disease progression This is near by results of (Velerti et al., 2006)⁽⁶⁾, a research work on 87 patients with non early HCC treated by combined TACE-RF for lesion

Our study showed moreover spacing between the two procedures relatively less procedure related complications, less hospital stay keeping even made combination therapy still an out patient procedure. TACE followed by RFA expressed less procedure related complications compared to RFA followed by TACE in terms of; for TACE followed by RFA group, post embolization syndrome experienced in 70%, revisable liver cell impairment in 10% and 0% had partial portal vein thrombosis while for RFA followed by TACE group, post embolization syndrome experienced in 80% and revisable liver cell impairment in 30%. The results are in same way with (Saeed AS, et al., 2010)⁽⁹⁾.

The study employed RFA as a sequential combination modality patients previously

underwent as TACE group developed marginal recurrence or newly developed lesion at different hepatic segment, by end of one year the results revealed; complete response achieved in (0%) of patients, partial response in (20%) while (30%) developed disease progression. The results agree with (Fotios L, et al., 2009)⁽⁴⁾ confirmed that the use of RFA results in a high rate of complete necrosis in HCC (80-90%) concerning lesions smaller than 2cm in diameter, while the majority (70-90%) of tumor residues were observed in patients with lesions larger than 3cm. of tumor size around 2 cm diameter revealing complete response in 77.4%, partial response in 10.8% and progressive disease in 21.7%.

Starting actual combination by RF ablation get benefits of perilesional hyperaemia for greater concentration of the chemotherapy delivered by TACE at the tumor periphery having nearly the same effect of ischemia before RFA induced by TACE. One year treatment outcome in RF followed by TACE group revealed; complete response obtained in 0%, partial response 10% and disease progression 30%. (Lencioni et al., 2001)⁽⁷⁾ have reported a successful percentage with objective response reaching (82%) among patients with HCC (lesion size variable between 2.8 and 7.0 cm) treated with TACE previously to RFA.

The current study employed TACE as a sequential combination modality patients previously underwent as RFA group developed multifocal or sizable recurrence, by end of one year the results revealed; complete response achieved in 20% of patients, partial response in 20%, and stable disease in 10% while 40% developed

disease progression. The results agree with (Cho YK, et al., 2009)⁽³⁾ who reported 48% objective response to TACE only group.

Conclusion

Actual combination modality of TACE followed by RFA is a treatment modality of choice that could be employed in different problematic HCC situations as lesions of size range 3-6cm diameter, morphology of ill defined tumor margins) or associated with small satellites in its vicinity.

TACE before RF has less hazards of complications regarding more spacing time between two procedures.

Sequential therapy of TACE post RFA or RFA post TACE could be employed for selected cases have HCC in size criteria of RFA and in cases with disturbed clinical performance or lab data.

References

1. Bolondi L, Gaiani S, Celli N, et al., Tumor dissemination after radiofrequency ablation of hepatocellular carcinoma. *Hepatology* 2001; 34: 608.
2. Bruix J, Sherman M; Practice Guidelines Committee, American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma. *Hepatology* 2000; 32(3): 1208-36.
3. Livraghi T, Goldberg SN, Lazzaroni S, et al., Hepatocellular carcinoma: radiofrequency ablation of medium and large lesions. *Radiology* 2000; 214(3): 661-68.
4. Rossi S, Garbagnati F, Lencioni R, et al., Percutaneous radio-frequency thermal ablation of nonresectable hepatocellular carcinoma after occlusion of tumor blood supply. *Radiology*. 2000; 214(1): 119-26.
5. Veltri A, Moretto P, Doriguzzi A, et al., Radiofrequency thermal ablation (RFA) after transarterial chemoembolization (TACE) as a combined therapy for unresectable non-early hepatocellular carcinoma (hepatocellular carcinoma). *Eur Radiol*. 2006; 16(3): 661-69.
6. Lencioni R, Cioni D, Donati F et al., Combination of interventional therapies in hepatocellular carcinoma. *Hepatogastroenterology* 2001; 48(37): 8-14
7. Mohamed WM, Saeed AS, Mohamed GEID, et al., Combined Radiofrequency Ablation and Transarterial Chemoembolization in Treatment of Unresectable Primary Liver Cancer. *Gastroenterol Hepatol* 2010; 2(3): 0043.
8. Fotios L, Evangelia S, Sophia M, et al., Computed Tomography-guided Radiofrequency Ablation of Hepatocellular Carcinoma: Treatment Efficacy and Complications. *J Gastrointestin Liver Dis* September 2009 Vol. 18 No 3, 323-328
9. Cho YK, Kim MY, Rhim H, et al., Systematic review of randomized trials for hepatocellular carcinoma treated with percutaneous ablation therapies. *Hepatology* 2009; 49(2): 453-9.