Radiofrequency Ablation Combined With Percutaneous Ethanol Injection in Treatment of Medium Sized Lesions 3-5 cm Hepatocellular Carcinoma

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Abstract: Purpose: We evaluated the therapeutic efficacy and survival of combination of percutaneous radiofrequency ablation (RFA) and percutaneous ethanol injection (PEI) for focal hepatic tumors 3-5 cm in diameter in patients with inoperable hepatocellular carcinoma (HCC). **Patients and methods:** Forty patients(29males and 11 females, median age 56.5 years, range 42-70 years) with single inoperable HCCs medium sized lesions 3-5cm in the longest diameter; Performance status according to eastern cooperative oncology group (ECOG) 0-2, with Child Pugh class A or B; All were randomized into 2 treatment arms; group A; Included 20 patients, who have received combined ultrasound guided local ablative cool-tip RF and PEI, and group B; Included 20 patients, who have received PEI only. All patients were followed up 4 weeks after the end of the ablative sessions by helical dynamic computed tomography for assessing the therapeutic response. 1, 2 year overall survival rates (OSR) and progression free survival rates (PFSR) were recorded. **Results:** The complete necrosis rate of lesions was (80%) for group A versus (65%) for group B; with no statistical significance difference (P >0.05). The 1, 2 year OSR were (75%), (55%) in group A vs. (60%), (40%) in group B, the 1, 2 PFSR were (60%), (45%) in group A vs. (45%), (25%) in group B with no statistical significance difference (P >0.05). The complications were tolerable and limited to pain, vomiting, liver abscess and bile duct dilatation. **Conclusion**: The combination of percutaneous radiofrequency ablation (RFA) and percutaneous ethanol injection (PEI) for focal hepatic tumors 3-5 cm was effective and safe with prolongation of survival in patients with inoperable hepatocellular carcinoma (HCC), with minimal tolerable complications.

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Key words: Hepatocellular carcinoma; Radiofrequency ablation; percutaneous ethanol injection.

Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancies in the world, and its incidence is increasing worldwide [1]. Although surgical resection or orthotropic liver transplantation (OLT) may provide the opportunity for a complete cure, only 5-10% of patients were candidate for surgical option due to underlying liver dysfunction with high incidence of tumor multiplicity. Therefore, percutaneous local ablation (PLA) now is considered the best treatment option; all clinical trials approved that local ablative procedures either percutaneous ethanol injection (PEI) or percutaneous radiofrequency ablation (RFA) were safe, minimally invasive, highly effective with prolonged survival that may equivalent to surgical option especially in early stage HCC[2]. PEI was beneficial in tumors less than 3cm in diameter and despite its advantage of being cheap, available, immediately toxic to tumor cells due to dehydration and intracellular coagulation leading to necrosis, fibrosis, thrombosis and vascular occlusion rather than it could approach the lesions in high risk location due to close proximity to various structures such as blood vessels, common bile duct, gall bladder, diaphragm or loop of intestine, but it had high local recurrence rate especially in tumors more than 3cm in diameter due to inhomogeneous distribution of ethanol because of presence of intralesional septa[3].

RFA induces thermal injury through delivery of electromagnetic energy as application of rapidly alternating RF current results in ionic agitation and frictional heat generation around electrode leading to coagulative necrosis due to denaturation of intracellular protein and melting of lipid bilayer depending on temperature degree that was above 60^{o}C and duration of heating that was vary according to the size of ablated lesion (8-15 min.) [2]. RFA showed lower local tumor progression rates and higher survival rates and could produce wider area of coagulative necrosis especially with the recent advances in RF generators and electrode design so it was more effective in HCC lesions more than 3cm[4]. But the main limitation of RFA was the risky location of tumors for fear of thermal injury as the heat generated around the electrode tip distribution all

directions and the disadvantage of the so called heat sink effect if lesion was near to major vessel [5].

So, combination of both procedures may strength the weak points of each and achieves larger area of coagulative necrosis especially for lesion 3-5cm or even more than 5cm, whatever tumor location and achieving more local control with improving the survival [6].

The Barcelona Clinic Liver Cancer system (BCLC) [7] that used as guidelines for staging HCC as it is useful in predicting outcomes and planning treatment, classifies patients with HCC into five categories depending on tumor status (size and number), liver function (Child Pugh scoring system), and performance status but with some limitation especially for tumors more than 3cm with good PS and had impaired liver function; (1) *Stage 0*[tumor size <2cm, Child A, PS 0]; treatment options are; a) resection if normal portal pressure and serum bilirubin, b) OLT if high portal pressure and high serum bilirubin level with negative major comorbidities, c) RFA or PEI if positive underlying liver disease.(2) *Stage A* [tumor size ≤3cm, No. ≤3 nodules, Child A-B, PS 0]; treatment options are; a) OLT if no associated liver disease, b) RFA or and PEI if associated with liver disease.(3) *Stage B*[Child A-B, PS 0, multinodular] treatment option is Combined modalities; Transarterial chemo-embolization (TACE) ± local ablative therapy. This stage needs further refinement and sub-stratification. (4) *Stage C*[Child A-B, PS 1-2, N1, M1]; sorafinib is advised.(5) *Stage D*[Child C, PS 3-4]; best supportive care is recommended.

So PLA is now considered the best treatment option for patients with Child–Pugh class A/B cirrhosis, ECOG performance status of 0–2, tumor ≤5 cm, solitary focal nodular lesion, and the main contraindications include the presence of vascular invasion, extrahepatic metastatic disease, sepsis, severe debilitation, Child–Pugh class C cirrhosis and uncorrectable coagulopathy[2,8].

2. Patients and Methods

Eligibility:

Forty patients with primary single focal hepatic lesion proved by helical dynamic computed tomography and a serum alpha-fetoprotien more than 200 IU/ml, who met the following eligible criteria were enrolled into the study: informed consent, age from 18-75 years, ECOG performance score of 0-2, single lesion sized 3-5cm in the longest diameter, child –Pugh class A or B cirrhosis, platelet count more than 50,000/μL, total leucocytic count more than 3000/μL, prothrombin time ratio more than 60%, serum albumin not less than 2.8g/dl, serum bilirubin not more than 3mg/dl, adequate renal function (serum creatinine ≤ 2 mg/dL). The exclusion criteria included; presence of vascular invasion, extrahepatic metastatic disease, sepsis, severe debilitation, Child–Pugh class C cirrhosis, uncorrectable coagulopathy and receiving previous treatment for HCC.

Patient assessment:

All patients had pretreatment evaluation, including complete medical history and full physical examination, assessment of performance status using ECOG performance score, laboratory investigations including; complete blood count (CBC), complete liver functions test (LFT), kidney function test (KFT), virological profile of HCV and HBV and serum AFP. Radiological studies were routinely done including chest x-ray, pelvi-abdominal ultrasonography and helical dynamic computed tomography, isotopic bone scan when indicated.

Treatment Schedule:

All patients were allocated into two groups; the combined RFA and PEI arm (Group A): included 20 patients (14 males and 6 females; mean age of 57.3 ± 6.4 years with range (44-69 years) who have received combined PEI of 95% ethyl alcohol followed by RFA for lesion size ranged from 3.2 to 5.0cm (mean size of 4.2 ± 0.6 cm), 8 patients with child A and 12 with child B, 80% of patients had HCV, while the PEI arm (group B): included 20 patients(15 males and 5 females; mean age of 57.6± 8.2years with range 42-70 years), who have received PEI only for lesion size ranged from 3.1 to 4.9cm(mean size of 4.0 ± 0.5cm), 9 patients with child A and 11 with child B, and 75% of patients had HCV.

Radiofrequency Ablation and Percutaneous Ethanol Injection Procedure:

All patients included in this study were injected in Zagazig University Radiodiagnosis Department, under complete aseptic condition, for local anesthesia, we injected 2% lidocaine hydrochloride at the puncture site, in addition 50mg of pethedine hydrochloride mixed with 50ml 0.9% saline was dripped by intravenous infusion for pain control during procedure, after local anesthesia, RFA needle with an electrode of 3cm in length was first introduced into the tumor under ultrasound guidance then spinal needle 20 f was inserted through the same hole of the attachment beside the echo probe, then part of ethanol 95% was injected slowly in the center of the lesion then the needle was withdrawn gently and repositioned in the periphery of the lesion to complete injection of about 8-12 ml of ethanol for each session (the total amount of ethanol was determined according to the equation:

$V\ (ml) = 4/3\mu(r+0.5)^3$

Where V represents the volume of ethanol (ml) and r represents the radius of the tumor in cm.

After 5minutes, the RFA procedure was started by using RF 200-W generator, where the ablation was started with 30 W of power output followed by a stepwise increase of 20 W every 3 minutes aiming to increase the temperature of the lesion up to 100ºC, multiple overlapping ablations were applied to achieve an adequate ablative margin at least 0.5cm, when the procedure was finished the power output was maintained at 50W while withdrawing the electrode needle to ablate the needle track to prevent tumor seeding, the whole procedure time was ranged from 18-32 minutes.

Generally, the PEI treatment session was repeated twice weekly according to tumor size and until changes in the tumor echogenicity was occurred.

Response and toxicity criteria:

The laboratory investigations were done weekly during treatment and monthly during the period of follow up including; complete blood count (CBC), liver functions test (LFT), kidney function test (KFT) and serum AFP level assessment for assessing the treatment response and side effects.

After 4 weeks of the end of local ablative procedures in both arms, all patients under went helical dynamic computed tomography for assessing the therapeutic response and every 3 months thereafter as well as ultrasonography to assess the size and echogenicity and other sonographic finding, along the follow up period. Tumor necrosis was considered complete if no enhancing areas were observed during early and late phases of helical dynamic computed tomography.

Response criteria as defined by *WHO* [9]were used; complete response (CR) was defined as the disappearance of all known disease on C.T as determined by two observations not less than 4 weeks apart, partial response (PR) was defined as more than 50% reduction in the product of the two largest perpendicular diameters of the tumor lesion, no response (NR) was defined as 50% decrease in total tumor size cannot be established or has a 25% increase in size of one or more measurable lesion, progressive disease (PD) was defined as more than 25% increase in the size of measurable lesions or the appearance of new lesions. Treatment toxicities were evaluated using the common toxicity criteria of the national Cancer Institute [10],

Statistical methods:

Data were presented as mean ± standard deviation (SD), median, range for quantitative variables and number and percentage for qualitative variables. Comparison of variables between the two groups was performed by the Chi-square test, Fisher exact test and student's t test [11]. The Kaplan-Meier method was used for survival analysis and the log rank test was used to compare between survival curves [12]. Survival times were calculated from the date of registration to the date of death and patients last known to be alive were censored at date of last contact, progression free survival times were calculated from the date of registration to date of first documentation of progression. Statistical significance was accepted as a *p*- value of less than 0.05.

3. Results

Patient characteristics:

This study included 40 patients with primary single focal hepatic lesion proved by helical dynamic computed tomography and serum alpha-fetoprotien >200 IU/ml, presented to Clinical Oncology and Nuclear Medicine Department, Zagazig University Hospitals, during period from July 2010 to January 2013.

Ninety percent of all patients were in the 5th and 6th decades of life with range (42-70 years), 29 patients were males representing 72.5% of all patients, all patients had ECOG performance score of 0-2, 42.5% of all patients presented with Child-Pugh class A; 8 patients (40%) in group A and other nine (45%) in group B, 80% of patients in group A and 75% of patients in group B had HCV, and 10% of all patients had both HBV & HCV, the mean lesion size was 4.2±0.6 cm in group A and 4.0±0.5 cm in group B, the number of sessions ranged 1-2 sessions with mean of 1.3±0.4, the duration of RFA session ranged 18-32 minutes with mean of 25±6.2 minutes in group A, while it ranged 3-6 sessions with mean of 3.9±1.1 in group B, the amount of injected ethanol was ranged 10-24 ml representing 26.1% of calculated amount in group A, while the amount of injected ethanol was ranged 24-84 ml representing 71.4% of calculated amount in group B, that has been recorded according to changes in tumor echogenicity (Table1).

Treatment response:

The complete ablation was achieved in 16 patients (80%) in group A versus 13 (65%) in group B (P>0.05) and was 100% in all child class A in both groups. In group A; 11/16 (68.8%) of completely ablated patients maintained the response; Fig. (2), 3/16 (18.8%) had local progression and 2/16 (12.5%) had multifocal recurrence away from the primary lesion, while in group B; 7/13 (53.8%) of completely ablated patients maintained the response, 4/13 (30.7%) had local progression and 2/13 (15.4%) had multifocal recurrence. All partially ablated patients in both groups had recurrence; 3 patients in group A and 5 in group B had local progression, while one patient and other two had multifocal progression in group A and B respectively.

The difference between both groups was statistically insignificant. Table (2).

Treatment complications:

There were different complications after injection in both groups; In spite of good analgesia before and during injection, 70% and 65% of patients experienced tolerable pain in group A and B respectively, five patients in each group had intolerable pain and were given strong analgesic (ketrolac amp.) with good response, only 15% in group A and 10% in group B had mild to moderate fever after injection and responded to usual antipyretics, also 20% and 15% in group A and B respectively experienced mild vomiting that recovered without medical interference, bile duct dilatation was recorded in 4 patients (20%) in group A and in 6 (30%) in group B, liver abscess was developed in one patient in each group and hemopeumothorax in another one in group A, with statistical insignificant difference. Table (3).

Survival:

The one and two year overall survival (OSR) was 75% and 55% in group A versus 60% and 40% in group B, while the 1,2 year progression free survival rate (PFSR) was 60% and 45% in group A versus 60% and 40% in group B, without statistically significant difference ($P > 0.05$). Follow up period time was ranged 12-32 months with mean of 26.1±6.5 in group A versus 11-28 months with mean of 22.4±7.8 in group B.

Subgroup analysis as regard Child-Pugh classification resulted in 1, 2 year OSR, (87.5%), (62.5%) versus (66.7%), (55.5%) in patients with child A, and (66.7%), (50%) versus (54.5%), (27.2%) in patients with child B in group A and B respectively. ($P >0.05$).

At the end of first year follow up, five of eight patients in group A, who developed disease progression, were died due to liver cell failure, versus eight of eleven patients in group B, died due to the same cause, during second year follow up, another three in group A, were died due to liver cell failure and one patient had been lost, while in group B; another 4were died due to liver cell failure, no patients in group B still alive at 30 months follow up versus 6 patients were still alive in group A, but this differences were statistically insignificant. Table (4), Fig. (1).

Table (1): Patient characteristics

Characteristics	Group A RFA and PEI (20 patients) NO. (%)		Group B PEI (20 patients) NO. (%)		*P*- value
Age in years Mean±SD Range	57.3±6.4 44-69		57.6±8.2 42-70		0.862
Sex Male Female	14 6	(70%) (30%)	15 5	(75%) (25%)	0.792
Child-Pugh class A B	8 12	(40%) (60%)	9 11	(45%) (55%)	0.736
Size(cm) Mean±SD Range	4.2±0.6 3.2-5.0		4.0±0.5 3.1-4.9		0.898
Virology HBV HCV Both	3 16 1	(15) (80) (5)	4 15 1	(20) (75) (5)	0.873
Number of treatment sessions Mean Range	1.3±0.4 1-2		3.9±1.1 3-6		0.084
% of injected ethanol to total calculated ethanol	26.1		71.4		0.064

Abbreviation: RFA; radiofrequency ablation, PEI; Percutaneous ethanol injection, SD; standard deviation

Table (2): Ablation Rate and response

	Group A RFA and PEI		Group B PEI		*P*-value
	No	%	No	%	
Ablation Rate					
Complete ablation	16	80	13	65	0.436
Partial ablation	4	20	7	35	
Response Rate					
Completely ablated (n.16)			Completely ablated (n.13)		
Stationary	11	68.8	7	53.8	0.518
Local progression	3	18.8	4	30.7	
Multifocal	2	12.5	2	15.4	
Partially ablated(n.4)			Partially ablated(n.7)		
Stationary	0	0	0	0	0.722
Local progression	3	75	5	71.4	
Multifocal	1	25	2	28.6	

Table (3): Complications after injection in both groups

Complication		Group A(n.20) RFA and PEI		Group B(n.20) PEI		*P*-value
		No	%	No	%	
Pain	Tolerable	14	70	13	65	0.688
	Intolerable	5	25	5	25	
Fever		3	15	2	10	0.623
Vomiting		4	20	3	15	0.638
Peritoneal collection		1	5	1	5	1.00
Hemopneumothorax		1	5	0	0	0.311
Liver abscess		1	5	1	5	1.00
Bile duct dilatation		4	20	6	30	0.423

Table (4): Survival Rate

	Group A(n.20) RFA and PEI		Group B(n.20) PEI		*P*-value
	No	%	No	%	
Mean follow- up period(months)	26.1±6.5		22.4±7.8		0.712
1-year OSR	15	75	12	60	0.417
2-year OSR	11	55	8	40	0.334
1-year PFSR	12	60	9	45	0.355
2-year PFSR	9	45	5	25	0.278
Abbreviation: OSR; overall survival rate, PFSR; progression free survival rate					

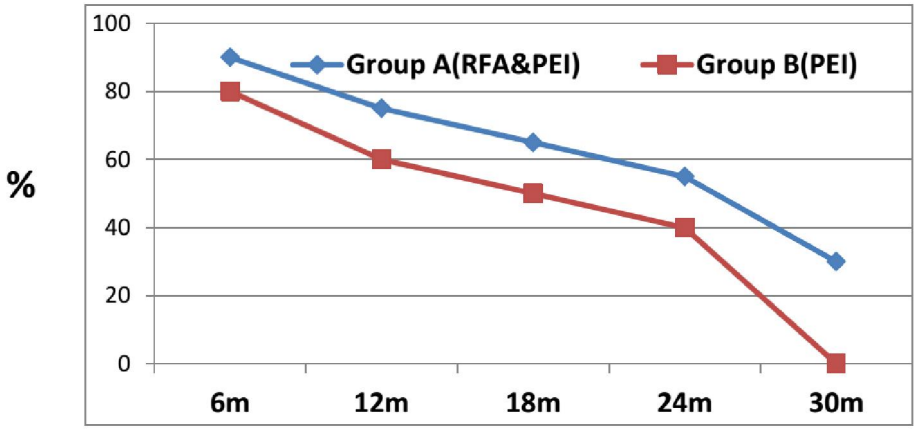

Figure (1): Overall survival rate in group A and group B

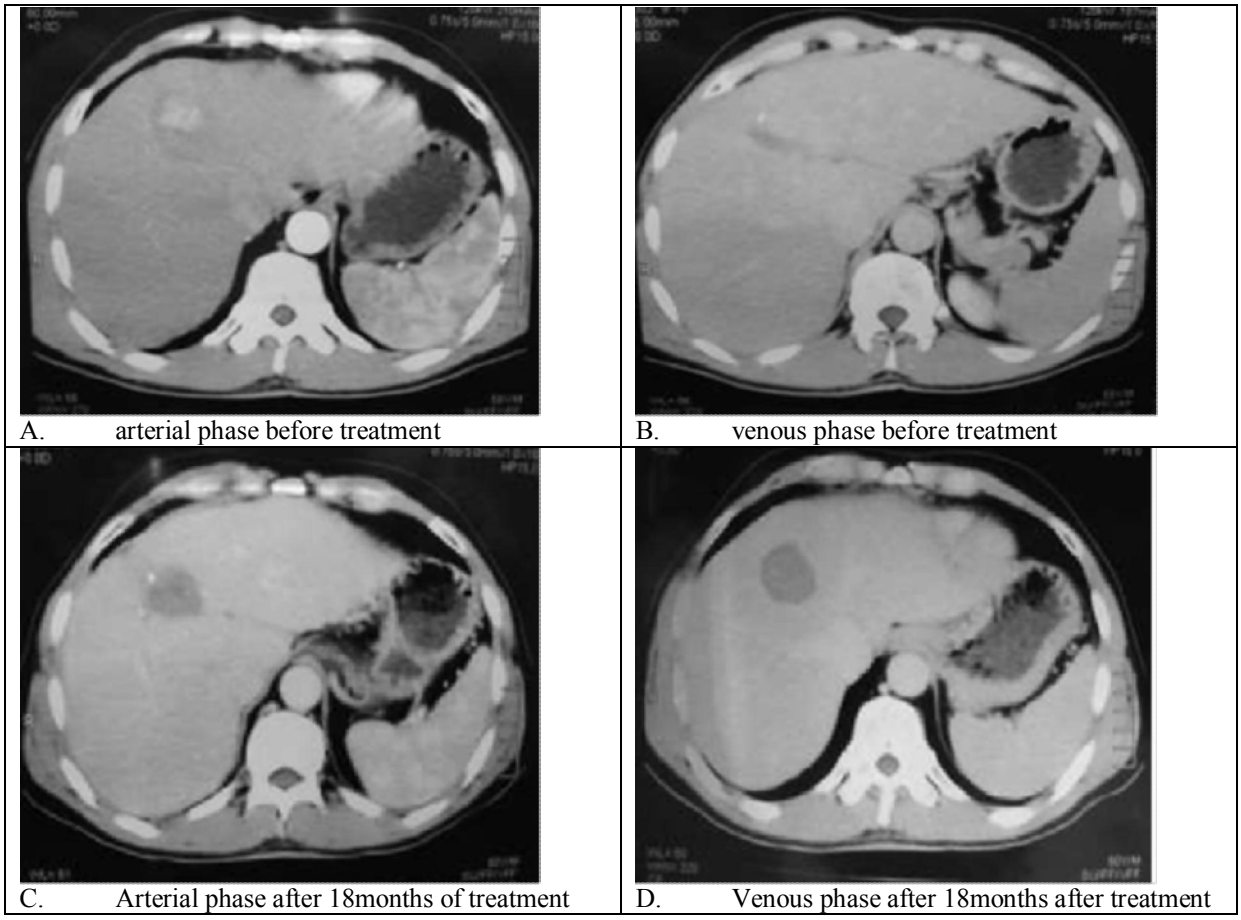

Fig. (2): Dynamic computed tomography of patient with single focal Rt. Lobe lesion before and 18 months after combined ablation therapy showed complete ablation necrosis.

4. Discussion

Hepatocellular carcinoma is one of the most common malignancies in the world, and its incidence is increasing worldwide, especially in South Africa and Eastern Asia [13]. Although surgical resection or orthotropic liver transplantation (OLT) may provide the opportunity for a complete cure, its role is limited due to underlying liver dysfunction as well as tumor

multiplicity. Therefore, percutaneous local ablation (PLA) now is considered the best treatment option; all clinical trials were approved that local ablative procedures either percutaneous ethanol injection (PEI) or percutaneous radiofrequency ablation (RFA) were safe, minimally invasive, highly effective with prolonged survival that may equivalent to surgical option especially in early stage HCC[5].

RFA is aiming to induce thermal coagulative necrosis and protein denaturation by producing frictional heat within tumor tissue as a result of ionic agitation when high frequency current is generated via needle electrode connected to RF generator, but the main obstacle for success is heat sink effect when tumor is close to main branches of portal and hepatic veins, and if tumor location near vulnerable structures as loop of intestine or central bile duct. [14]

PEI using absolute alcohol is aiming to induce cellular dehydration and occlusion of blood vessels leading to tumor necrosis, but presence of intralesional fibrous septa, resulting in inhomogeneous diffusion of alcohol inside tumor tissue leading to high recurrence rate especially in tumors sized more than 2 cm as mentioned in many clinical trials. [15]

So, combination of both modalities could strength each other and may be used in lesions more than 3 cm whatever its location, also this combination will reduce the total amount of injected ethanol minimizing the number of sessions and also abolish the heat sink effect that elongates the duration of RF ablation time, achieving high ablative rate minimizing the chances for recurrence that have modest influence on overall survival rates.

In present study, all patients had mean age of 57.5±7.3 years with age range of 42-70 years which was very close to that reported by Cha *et al.*[5]; (59.4±9.6 years), and lower than reported by Kurokohchi *et al.* [16]; (69 years) with age range of 44-86 years, and Lin *et al.* [17]; (64.2 years), with male predominance accounting for 72.5%, which was close to that stated by Kurokohchi *et al.* [16]; (73.3%), and higher than reported by Cha *et al.* [5]; (65%), and Lin *et al.* [17]; (61.4%).

According to Child-Pugh scoring system; 42.5% of all patients in our study were Child A, which was close to that stated by Kurokohchi *et al.* [16]; (60%), but was very lower than that reported by Cha *et al.* [5] as his study mentioned that all patients were Child A, the rest of our patients were Child B representing 57.5%.

In our study, all lesions size ranged 3.1-5.0 cm whereas the mean size in group A was 4.2±0.6 cm that was higher than reported by Kurokohchi *et al.* [16] as his work was on lesions with mean size of 3 cm when use the same combined modalities, and also Cha [5] and his coworkers when use the combined methods on lesions with mean size of 2.1±1.3 cm, while Luo *et al.* [6] treated 24 patients by RFA after PEI for lesions ranged 3.5-7.2 cm with mean of 5.4±2.8 cm.

As regard the number and duration of sessions; in group A, the number of sessions ranged 1-2 sessions with mean of 1.3±0.4, that was comparable to what reported by Cha *et al.* [5]; 1.1±0.4, Kurokohchi *et al.* [16] work on 60 patients by combined modalities with mean of one session, Luo *et al.* [6]; (mean, 2.1 sessions) but in group B, it was 3-6 sessions with mean of 3.8±1.4. The duration of session in group A was ranged 18-32 minutes with mean of 24.6±4.2 minutes; that was comparable with that reported by Ragesh *et al.* [2] as the duration of session ranged 15-30 min. and slightly higher than reported by BCLC group [18]; 22.1 min. as they worked on lesions ≤ 3cm with mean no. of sessions 1.25, while Fayed and his associates [19] recorded duration of session 26 min. with mean no. of sessions 2 when use RFA on lesions ≤ 5 cm.

In our study, the amount of injected ethanol was 26.1% of total calculated ethanol versus 71.4% in group A and B respectively, these difference had tendency to be significant (*P* value 0.064), that was close to that reported by Cha *et al.* [5] as the difference between the amount of injected ethanol in combined arm versus PEI arm reached significance (*P* value 0.03) but he worked on tumor size (2.1±1.3 cm) in combined arm versus (1.5±0.3 cm) in ethanol arm, while size of lesions in our study was (4.2±0.6 cm) in combined group versus (4.0±0.5 cm) in ethanol group, and this means that combination of PEI and RFA was greatly minimized the number and duration of session beside it also reduce the amount of injected ethanol for achieving the complete ablation rate that reached 80% in group A versus 65% in group B in our study. In addition the heat sink effect due to risky location of lesions that lie within 5mm of major vein >3mm in diameter or vital structure [GIT, GB, CBD and lung] that was the major drawback for complete ablation significantly had overcome by PEI as mentioned by Teratani *et al.* [20].

As regard the efficacy of treatment; in our study, the complete ablation rate was recorded in 16 patients (80%) in group A versus 13 (65%) in group B and this difference was statistically insignificant, but higher than reported by Luo *et al.* [6]; as he achieved complete necrosis rate 57.7% when used combined modalities in 52 patients with HCC lesions ranged 3.5 to 7.2 cm that are larger than our lesions size (3-5 cm), also he reported 77.6% complete necrosis rate when used only PEI in 85 patients but with small sized lesions ranged 1.3 to 2.9 cm, this explain why our result in ethanol group was lower (65%). Also our result was lower than reported by Cha et al[5]as he achieved 100% complete necrosis rate with local tumor progression

rate of 12.5% (1/8) in comparison with our results 25% (5/20)and these were attributed to small sample size and smaller lesions size (0.8-3.4 cm).

The toxicities related to our treatment was tolerable and controlled ranged from pain that was intolerable in 25%, fever in 12.5%, vomiting in 17.5% of all patients and all were responded to usual medication. Liver abscess was recorded in 5% (1/20) in both groups while Cha *et al.* [5] recorded 12.5% (1/8) in combined group and 0% in PEI group, bile duct dilatation was recorded in 25% (2/8) versus 20% (4/20) for combined modalities in our results.

In our study, the median follow up time was 26.1±6.5 and 22.4±7.8 months and 1- and 2- year OSR were 75% and 55% versus 60% and 40%, mean while1- and 2- year PFSR were 60% and 40% versus 45% and 25% in groups A and B respectively and these differences were statistically insignificant, our results was slightly higher than that reported by Luo *et al.* [6]; as 1- and 2- year OSR were 68.6% and 46.2% for combined RFA and PEI, and lower than his results for ethanol only 80% and 60%in his study, and as we mentioned before this was attributed to lesion size. But slightly lower than reported by Shi *et al.* [25]as he recorded 1- and 3- year OSR; 88.2% and 58% and 1- and 3- year PFSR; 87.9% and 57.6% and these difference because of the lesions sized in his study were less than 4 cm. The mean follow up periods were comparable with that recorded by Cha *et al.* [5] 24.5±9.4 months for combined modalities and 23.6±10.8 months for PEI only.

Our OSR was lower than reported by Zhang *et al.* [26], as 1 year OSR was 96% and 2 year OSR was 88% for combined modalities when he treat lesions 3.1-5 cm and it was 91.7%, 82.9% for lesions 5.1-7 cm but his final result revealed that 3 year OSR was significantly higher for RFA-PEI for lesions 3.1-5 cm than those for 3cm or smaller or those with 5.1-7 cm tumors.

Also, Sun *et al.* [27], reported that when he used the two modalities on lesions sized 3-5 cm, it was better when PEI was preceded RFA by 1-2 weeks than when RFA was applied first or the two modalities were done simultaneously as the volume of tumor ablation necrosis was significantly greater in PEI first then RFA than others. These results were reflected on OSR as it was 77.1% in group PEI then RFA versus 48.5% and 53.1% for others respectively.

Conclusion

In conclusion, our study showed that the addition of RFA to PEI achieves larger area of coagulated necrosis especially for lesion 3-5cm, whatever tumor location and achieving more local control with improving the survival, and as well as the volume of coagulated necrosis was four times larger than RFA alone because ethanol injection prior to RFA equally enhance the volume of coagulated necrosis in 3 dimensions to the same extent, as mentioned by Kurokohchi *et al.* [6] also, the energy required for ablation was ¾ of that in RFA only.

Conflict of interest (none)

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