Percutaneous radiofrequency ablation compared with surgical resection in the treatment of early hepatocellular carcinoma

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Objective
The primary objective of this study was to compare between liver resection (LR) and radiofrequency ablation (RFA) in the management of early hepatocellular carcinoma (HCC). We are trying to provide an update that can be valuable in clinical practice for determining the most suitable first-line management option for early HCC.

Patients and methods
The study included 80 patients with early HCC according to the Barcelona Clinic Liver Cancer staging system. Patients were divided into two groups: group A included 40 (50%) patients treated through LR, whereas group B included 40 (50%) patients managed through percutaneous RFA. In this study, we used the alternation method as an allocation process in this study. Procedures in both groups were done according to conventional principles. Percutaneous RFA technique was done under the guidance of ultrasonography (US) in complete aseptic conditions. Collected data included procedure time, intraoperative bleeding, postoperative complications, pain score, ICU, and the total hospital stay days. After procedures, patients were monitored every three months throughout the follow-up period.

Results
A total of 80 patients with early HCC underwent treatment with LR (N=40) and with RFA (N=40). There is a significant difference between both groups regarding the mean time of the procedure: 145±19.8 versus 40.6±7.8 min for LR and RFA, respectively. Rates of recurrence significantly ($P<0.05$) correlated with age and tumor size in both groups. No significant difference was observed in rates of recurrence or the time of recurrence ($P>0.05$) between LR and RFA groups. However, the recurrence percentage was slightly higher among patients treated by RFA compared with LR group.

Conclusion
Our prospective comparative study offers evidence that RFA provides a novel treatment for early HCC, and it shows survival and tumor relapse rates comparable to LR.

Keywords:
hepatocellular carcinoma recurrence, liver resection, percutaneous radiofrequency ablation

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Introduction

Hepatocellular carcinoma (HCC) is one of the most common cancer worldwide [1]. It accounts for ~90% of primary liver tumors. It is the primary leading reason of the global cancer-related mortality [1]. Follow-up plans for patients with chronic liver disease together with advanced diagnostic technologies have led to the rising figures of patients with HCC diagnosed at an early stage [2]. In Egypt, according to the national cancer institute, HCC represents 11.75% of all gastrointestinal tumors and 1.7% of entire malignancies [3]. There are many systems for staging HCC. However, Barcelona Clinic Liver Cancer (BCLC) is the most common staging system to be advised by the European and the American Associations for the Study of Liver Diseases [4].

Options for management of HCC are variable, and the decision on the most suitable line of treatment should be made by a multidisciplinary team [5]. No particular treatment plan can be useful for all patients, and treatment should be personalized [6]. Currently, liver resection (LR) is the first choice treatment for achieving a potentially reasonable long-term outcome in patients with HCC [7]. However, most primary HCCs are not appropriate for LR at the time of presentation [8]. Consequently, numerous nonsurgical procedures have been established, such as percutaneous ethanol injection,

radiofrequency ablation (RFA), transarterial interventions, radiation, chemotherapy, gene therapy, and immune therapy [9]. Among these, RFA has been the most broadly beneficial choice for unresectable HCC as well as it is harmless, with negligible morbidity and mortality [10]. Nowadays, percutaneous RFA is considered a standard care for patients with early-stage HCC not a candidate for surgery, but still, there are controversies about the possibility of RFA to compete with surgery as a first-line management in the treatment of HCC, and outcomes of studies on this issue are still inconsistent [11]. In our present work, we are trying to compare between percutaneous RFA and LR as a principal treatment for potentially resectable HCC.

Patients and methods

The current study was conducted at the General Surgery Department, Internal Medicine Department, and Hepatology, Gastroenterology and Infectious Diseases Department, at Banha University Hospital in Egypt and King Saud Hospital in Saudi Arabia from May 2013 till August 2017. Our study included 80 patients with early HCC according to BCLC staging system. After obtaining written fully informed consent, patients were admitted for clinical evaluation, performance status (PS), laboratory assessment [α-fetoprotein (AFP), hepatitis markers, liver function tests, complete blood count, coagulation profile, and routine biochemistry), abdominal ultrasonography with duplex study to detect the relation of the tumor to major blood vessels, and triphasic computed tomography (CT) or MRI for assuring the diagnosis and delineate the relation with blood vessels. PET scan was done for the identification of extrahepatic metastases. All patients underwent upper gastrointestinal tract endoscopy for detection of esophageal or gastric varices.

Inclusion criteria included the following: patients with a solitary liver nodule 5 cm or less, ECOG PS of 0–1, platelet count more than 100 000/mm^3, no vascular invasion, no extrahepatic spread, and patients in class A according to the Child–Pugh classification of liver disease severity. Exclusion criteria included the following: multinodular hepatic lesions, solitary nodule more than 5 cm, vascular invasion, extrahepatic spread, Child–Pugh class higher than A, ECOG PS of 2–4, and recurrent cases either after LR or RFA. All enrolled patients were clinically examined for demographic data, including age, sex, accompanying morbidities, tumor characteristics (location; either right or left lobe and tumor size), hepatitis viral infection B and/or C, presence or absence of cirrhosis, presence or absence of portal hypertension, Child–Pugh classification, and tumor staging according to BCLC. Patients were classified according to the type of management provided as either LR (group A) or percutaneous RFA (group B). Procedural and postprocedural data were collected. In this study, we used the alternation procedure as an allocation process, which is not dependent on anyone's personal decision. In this method, we performed LR for the first patient who was involved in the study, then percutaneous RFA to the second patient, then LR to the third patient, and so on.

Management plans

Liver resection group

Operations were completed according to conventional principles after admission. Patients' condition was evaluated to detect any intolerable risk, according to the American Society of Anesthesiologists grades III to V. Operations were done under general anesthesia. With the patient in supine position, a right subcostal incision with a midline extension to the xiphoid process was made, and an extension to the left subcostal area was sometimes done to provide further exposure. Once the abdomen was opened, we explored for possible ascites, metastasis, or other tumors. The liver was palpated bi-manually and examined by intraoperative ultrasonography to detect any mass not diagnosed before, and delineate tumor margin, and through duplex study, we can reassess any vascular invasion. Porta hepatis and celiac area was examined for any palpable lymph nodes. The liver is fully mobilized by separating all ligamentous attachment. The liver inflow is temporarily controlled by clipping the hepatoduodenal ligament (Pringle maneuver). The line of transection was marked with electrocautery with a safety margin of 1 cm in the cirrhotic liver and up to 2 cm in the noncirrhotic liver around the tumor; the parenchyma was then transected using the harmonic scalpel device (Ultracision; Ethicon Endosurgery, Cincinnati, Ohio, USA). The specimen was removed, and the raw surface area was then examined for any bile leakage or bleeding; if any, it was secured with absorbable suture over blunted tip needle and hemostatic synthetic material. The drain was kept near the raw area. The abdominal wound was closed in layers. After surgery, patients were shifted to ICU if needed. Postoperatively, patients received intravenous fluids, analgesics, packed red blood cells (when hemoglobin$<$7 g%), fresh frozen plasma [when prothrombin time (PT)$>$17 s], intravenous human albumin (when serum albumin$<$3 g%), and spironolactone (when there was lower limb edema). Oral feeding was resumed gradually.

Percutaneous radiofrequency ablation group

The imaging tools required for RFA comprise the equipment essential for US and RFA tools itself, which has three chief elements: needle electrodes, grounding pads that are attached to the patient's thigh or back, and electrical generator. The alternating electric current generator is of 200 W operated at 480 kHz. The Radio Therapeutics RF2000 RFA system (model 3E; Radionics, Burlington, Mass) was used with a 3.5-cm LeVeen ablation needle (SMK Electrode; Cosman Medical, Burlington, Mass). The needle electrodes of RFA include a 14-G insulated outer needle that comprises nine retractable curved electrodes of various lengths. A single pin or 2–4.0 cm diameter umbrella, ablation needle was carefully chosen according to tumor size and location.

The technique of radiofrequency ablation

Percutaneous RFA procedures were done as a day-case set. The position was as comfortable as possible to patients without interfering with the physician's capability to sufficiently see and manage the tumor. The RFA was accomplished with local anesthesia and mild intravenous sedation when needed. Under complete aseptic condition, the ablation needle positioned directly into the proposed tissue under US guidance. One or additional electrodes emerged from the tip of the needle inside the tumor. The generator switched on RF energy currents through the electrodes and leads to ionic agitation. This agitation and friction of ions produce heat, and the high temperature destroys the intended tissue. Minute thermometers fixed into the ends of the electrodes permit continuous checking of tissue temperatures. Power is automatically accustomed so that the intended temperatures stay fixed. As tissue temperature rises over 50°C, cell protein is destructed forever and coagulation necrosis begins. Over 60°C, cell death happens virtually promptly. Nearly 15–30 min is needed to perform a 3–5 cm tumor ablation. Ultrasonography was used to observe the procedure through changing (increasing) of tissue echogenicity. These US changes, owing to the creation of vapor bubbles from the ablated tissue, are used as a rough calculation of the size of the ablated tissue. When tumor size is more than 3 cm, several ablations were done to reduce the possibility of local tumor relapse. After satisfactory US changes, the needle electrode is removed and compression is applied to the skin entry site to stop any bleeding, and then the skin opening is protected with a sterile dressing without suturing.

Postprocedural care

Few patients complained of discomfort directly after the ablation sitting; this was resolved with oral painkillers. Patients were discharged 6 h after procedure. Patients were reassured about the possible complications and given contact numbers to call if they notice any problem. Some patients experienced the postablation syndrome (malaise, myalgia, low-grade fever, nausea, vomiting, and delayed pain), and it was self-limiting.

Follow-up of patients throughout the study period

In the first postoperative (PO) year, follow-up imaging comprised the use of US with colored Doppler and triphasic CT within a month of the procedure, and then every 3 months. In the case of effective ablation, the lesion shows no enhancement with contrast study with or without a hyperattenuating border. On the reverse, nodular and dense enhancement denotes a tumor relapse. Moreover, an AFP assay was done every month through follow-up. All investigations were done every 3 months during the second year of follow-up, and then every 6 months thereafter till the time of the study. If AFP ranks sustained rise and image readings did not specify relapse, chest CT with contrast and a whole body bone scan or PET scan were done. When a tumor relapse was identified, the patient was submitted to the committee of a multidisciplinary team to cultivate a new plan for treatment.

Statistical analysis

Obtained data were presented as mean±SD, ranges, numbers, and ratios. Results were analyzed using Wilcoxon's signed-rank test for related samples, ranked test for unrelated data (Z-test), and χ^2-test). Statistical analysis was conducted using the SPSS (version 19 for Windows; SPSS Inc., Chicago, Illinois, USA) statistical package. A P-value of less than 0.05 was considered statistically significant.

Results

The study included 80 patients with early HCC according to BCLC, and they were divided into two groups: group A contained 40 (50%) patients treated through LR and group B contained 40 (50%) patients managed by percutaneous RFA.

No significant difference between both groups was observed regarding age, sex, and clinical presenting findings. Most patients in both groups had underlining compensated chronic hepatic insults (class A according to the Child–Pugh classification). No significant difference between both groups was

found regarding hepatitis markers, underlining liver cirrhosis, portal hypertension, and serum level of AFP. Details of patients' enrollment data are shown in Table 1. Most tumors in both groups were located in the right hepatic lobe. No significant difference between both groups was observed regarding tumor size, number, and BCLC staging (Table 2).

Patients of both groups had uneventful operative/procedural complications, with a significant difference between LR and RFA about the mean operative time ($P<0.05$) and the mean intraoperative/procedural blood loss ($P<0.05$). Intraoperative/procedural data are summarized in Table 3. During the early PO/postprocedural period, there was a significant difference between LR group and RFA group regarding the mean hospital stay days ($P<0.05$), days of ICU admission ($P<0.05$), and the mean PO visual analogue scale (VAS) score ($P<0.05$); other PO/ablation data are shown in Table 4.

There is no doubt that tumor recurrence is the worst event following primary management of any malignancy, and it expresses clearly in terms of survival rates and tumor-free survival rates. In our present work, there is no significant difference in rates of recurrence between LR and RFA groups ($P>0.05$). The relation between tumor recurrence

Table 1 Studied patients' preoperative demographic data

Data	LR group	RFA group	*P*-value
Total (*n*=80)	40 (50)	40 (50)	
Age	48.51±7.12 (32–70)	46.35±9.60 (35–69)	NS
Sex			
Male	33 (82.5)	32 (80)	NS
Female	7 (17.5)	8 (20)	NS
Presenting symptoms			
Asymptomatic	19 (47.5)	17 (42.5)	NS
Abdominal pain	8 (20)	7 (17.5)	NS
Weight loss	13 (32.5)	13 (32.5)	NS
Jaundice	0	3 (7.5)	NS
HbsAg (positive)	18 (45)	20 (50)	NS
HCV-Ab (positive)	15 (37.5)	17 (42.5)	NS
Underlining liver cirrhosis	33 (82.2)	35 (87.5)	NS
Portal hypertension	10 (25)	8 (20)	NS
Hyperbilirubinemia	4 (10)	3 (7.5)	NS
Child–Pugh class A	40 (100)	40 (100)	NS
AFP (ng/ml)			
≥400	25 (62.5)	27 (67.5)	NS
<400	15 (37.5)	23 (32.5)	NS
ECOG performance status			
0	35 (87.5)	36 (90)	NS
1	5 (12.5)	4 (10)	NS

Data are presented as mean±SD and numbers; ranges and percentages are in parentheses. AFP, α-fetoprotein; LR, liver resection; RFA, radiofrequency ablation.

Table 2 Preoperative data of hepatic lesions

Data	LR group [*n* (%)]	RFA group [*n* (%)]	*P*-value
Total (*n*=80)	40 (50)	40 (50)	
Tumor location			
Right lobe	32 (80)	35 (87.5)	NS
Left lobe	8 (20)	5 (12.5)	NS
Tumor size (cm)			
2–3	10 (25)	8 (20)	NS
3.1–4	18 (45)	21 (52.5)	NS
4.1–5	12 (30)	11 (27.5)	NS
Tumor stage (BCLC)			
A1	21 (52.5)	19 (47.5)	NS
A2	10 (25)	8 (20)	NS
A3	9 (22.5)	13 (32.5)	NS

BCLC, Barcelona Clinic Liver Cancer staging system; LR, liver resection; RFA, radiofrequency ablation.

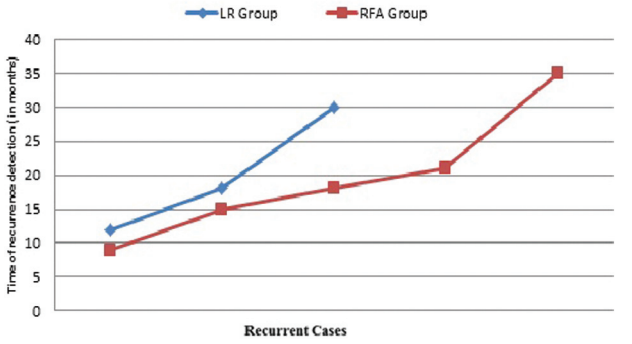
and the patients' enrollment data is mentioned in details in Table 5.

The frequency of recurrence, the time of detection of recurrent cases throughout the follow-up period, and the relation between time of recurrence, tumor size groups, and BCLC subgroup are illustrated in Figs 1–3.

Discussion

LR has regularly been established as the principal option for management of HCC in several oncology institutes with some criteria (a solitary tumor with a diameter≤5 cm or up to three lesions≤3 cm in diameter) [12]. Only 10–25% of patients with HCC are fit for surgery at the time of diagnosis owing to either reduced hepatic reserve because of underlying chronic liver illness or multiple hepatic lesions [13]. Therefore, several nonsurgical procedures have been

Figure 1



Frequency of recurrence detection throughout follow-up period. LR, liver resection; RFA, radiofrequency ablation.

Table 3 Operative/procedural data in both groups

Data	LR group [*n* (%)]	RFA group [*n* (%)]	*P*-value
Total (*n*=80)	40 (50)	40 (50)	–
Operative time (min)	145±19.8 (110–180)	40.6±7.8 (30–60)	<0.05
Blood loss (ml)	300±157 (150-700)	7±3 (5–15)	<0.05
The number of blood units used	1.77±0.83 (1–3)	0	<0.05
The number of entrances/setting			
1	–	13 (37.5)	–
2	–	11 (27.5)	
3	–	16 (40)	
Anesthesia			
LA only	0	25 (62.5)	–
LA+light sedation	0	11 (27.5)	
LA+deep sedation	0	4 (10)	
General	40	0	

Data are presented as mean±SD and numbers; ranges and percentages are in parentheses. LA, local anesthesia; LR, liver resection; RFA, radiofrequency ablation.

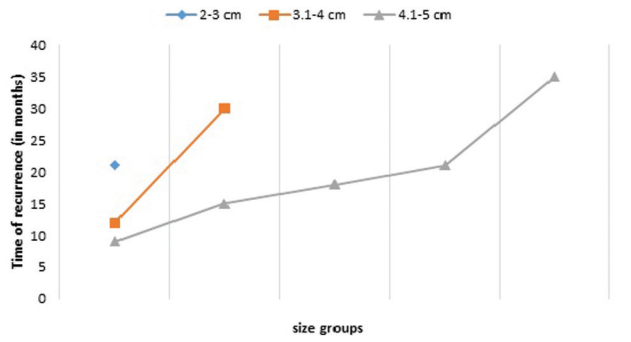
Table 4 The early postoperative/postprocedural data in both groups

Data	LR group	RFA group	*P*-value
Total (*n*=80)	40 (50)	40 (50)	
Hospital stay (days)	10.76±5.4 (5–20)	0.48±0.19 (0.25–2)	<0.001
PO ICU stay (days)	4.52±2 (2–9)	0	<0.001
PO pain (VAS score)	5.5±0.9 (4–7)	1.68±0.76 (1–3)	<0.05
Biliary leakage (minimal; subsided gradually)	2 (5)	0	NS
PO Bleeding (mild; managed conservatively)	5 (12.5)	2 (5)	NS
Liver failure	2 (5)	0	NS
Wound infection			
Cellulites	3 (7.5)	4 (10)	NS
Marked (need drainage)	1 (2.5)	0	NS
Liver abscess (3 weeks after ablation and drained under CT guidance)	0	1 (2.5)	NS
Fever	5 (12.5)	12 (30)	<0.05
Lower limb edema	6 (15)	0	<0.05
Chest problems			
Pleural effusion	0	2 (5)	NS
Pneumothorax	0	1 (2.5)	NS
Total number of PO complications	24	22	NS

Data are presented as mean±SD and numbers; ranges and percentages are in parentheses. CT, computed tomography; LR, liver resection; PO, postoperative; RFA, radiofrequency ablation; VAS, visual analogue scale.

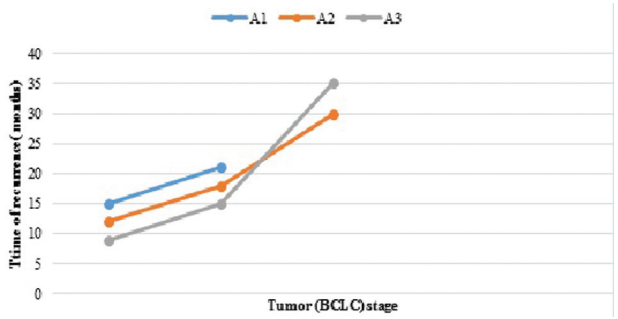
implemented. RFA is a hopeful ablation therapy among these techniques. RFA is less invasive, less expensive, and can be done as a day-case procedure [14]. Fundamentally, RFA is recommended for HCC nodules 3 cm or less in diameter where a regional control of tumor can be accomplished with only one application of RFA [14]. However, there is still debate on which is the superior in the treatment of HCC suitable for resection, RFA or LR [12]. Some studies reported that LR had more benefits in survival and relapse rates irrespective of tumor size less or more than 3 cm in diameter [15]. On the contrary, some researchers showed that LR was equal to RFA in the management of single and small HCC and recommended that RFA can be considered the gold standard treatment in such cases even when LR is feasible [15]. However, some studies mentioned that in patients with HCC between 3 and 5 cm in size, the success rate of RFA alone was unnoticeable. [16]. In our study, we proud to add our effort to other researchers in focusing the scope on the significant differences in outcome between RFA and LR in the treatment of HCC 5 cm or less in size, to reach conclusions concerning the efficiency of one of them as a first choice management plan. In our present study, the mean operative time needed for LR group was 145 ±19.8 min, and it is significantly higher than the time needed for percutaneous RFA 40.6±7.8 min. On the contrary, LR was implemented under general anesthesia [the risks of general anaesthesia (GA) cannot be ignored], whereas RFA was done under only local anesthesia in 25 (62.5%) cases with some sedation in 15 (37.5%) cases. We cannot deny the intraoperative complications during LR, such as blood loss with risks of blood transfusion, as happened in our study in four (10%) patients. On the contrary, in RFA, there were no intraprocedural hazards in our study group. This goes with Lei *et al.* [17], who concluded in his study that the mean operation time in LR was significantly higher compared with RFA, and they reported that long operation time and intraoperative events in LR have an inverse influence on the already unhealthy cirrhotic liver.

Figure 2



Frequency of recurrence time between cases in relation to size group.

Figure 3



Frequency of recurrence time between cases in relation to Barcelona Clinic Liver Cancer (BCLC).

Table 5 The rate of tumor recurrence in relation to patients' enrollment data

Data	Strata	LR group		*P*-value	RFA group		*P*-value
		N=40	Recurrence *n*/rate		*N*=40	Recurrence *n*/rate	
Age group	20–40	8 (20%)	1 (2.5%)	>0.05	7 (17.5%)	2 (5%)	>0.05
	41–60	27 (67.5%)	2 (5%)		26 (65%)	2 (5%)	
	>60	5 (12.5%)	0		7 (17.5%)	1 (2.5%)	
Sex	Male	33 (82.5%)	3 (7.5%)	<0.001	32 (80%)	3 (7.5%)	>0.05
	Female	7 (17.5%)	0		8 (20%)	2 (5%)	
Tumor (BCLC) stage	A1	21 (52.5%)	1 (2.5%)	>0.05	19 (47.5%)	1 (2.5%)	>0.05
	A2	10 (25%)	1 (2.5%)		8 (20%)	2 (5%)	
	A3	9 (22.5%)	1 (2.5%)		13 (32.5%)	2 (5%)	
Tumor size	2–3 cm	10 (25%)	0	<0.05	8 (20%)	1 (2.5%)	<0.05
	3.1–4 cm	18 (45%)	1 (2.5%)		21 (52.5%)	1 (2.5%)	
	4.1–5 cm	12 (30%)	2 (5%)		11 (27.5%)	3 (7.5%)	
Total recurrence			3 (7.5)			5 (12.5)	>0.05

Data are presented as numbers; ranges and percentages are in parenthesis. BCLC, Barcelona Clinic Liver Cancer; LR, liver resection; RFA, radiofrequency ablation.

In our study, no significant difference between LR and RFA groups was found concerning the primary postoperative/procedural outcome. In the LR group, immediate PO morbidity was reported, which varied from one patient to another, with a total number of 24 complications (some patients had more than one complication). On the contrary, most patients of RFA group passed non alarming PO time with a total number of 22 complications (some patients gain more than one complication). These figures of PO morbidity correlate with Yamazaki *et al*. [18], who reported that RFA results in a decline in PO morbidity incidence compared with the LR group (8.3 vs. 12%). However, numerous complications are particular for RFA, but with very low incidence, such as pneumothorax, pleural effusion, bleeding in the biliary ducts, and liver abscess [18]. The mean postprocedural pain VAS score for patients in ablation group was 1.68±0.76, and it is significantly lower than the mean VAS score in resection group (5.5 ±0.9), and of course, this gives more postprocedural satisfaction for patients in RFA group. This goes with Hong *et al*. [19], who reported that a shorter operation time, less blood loss, less pain, and a minimally invasive percutaneous ablation technique improve the PO recovery of patients. It was clear in our study that the unnoticeable PO morbidities in the RFA group led to a significant reduction in the length of hospital stay (0.48±0.19 days) compared with LR group (10.76 ±5.4 days). All these results reflect a significant reduction in medical costs of RFA in comparison with LR. In our study, no PO mortality was recorded in both groups.

Wang *et al*. [20] mentioned that there is no doubt that recurrence of the tumor is the most important issue that affects the survival and tumor-free survival of cases with small HCC. In our comparative analysis, we concentrated on the survival of patients who received RFA compared with patients who underwent LR. Cho *et al*. [21] mentioned that no significant variances were observed among RFA and LR in tumor-free survival rates and survival rates in cases with HCCs that not exceeding five cm in diameter. They attributed this to the advances in RFA techniques, equipment design, and good physician training [21]. This is in contrast to Jiang *et al*. [22], who stated that most of the present researchers have recommended that LR is superior to RFA because of the extent of a single ablation using RFA, which is a sphere-shaped area of around 4–5 cm. In addition, when the lesion is about 5 cm in size and irregular in shape, it is hard to totally destruct the surrounding zone of the lesion [22]. However, in the present study, RFA procedure was done under the guidance of the US with repeated RFA at numerous points to attain satisfactory ablation results of the tumor and clearance of 2 cm of surrounding hepatic tissue as a safety margin.

We agree with Cho *et al*. [21], as we also reported no significant difference in recurrence rates between the two groups ($P>0.05$); however, the recurrence rate was higher in the RFA group (12.5%) compared with 7.5% in the resection group. In patient managed with RFA, we reported a significant relation ($P<0.05$) between recurrence rate and tumor size. The rate of recurrence was 60% in lesions with tumor diameter 4.1–5 cm. This goes with Ikeda *et al*. [23] who stated that the effectiveness of RFA is extremely size dependent, and results of RFA for HCC 3 cm or less in diameter are obvious. In 2014, Huang *et al*. [24] reported the results of a randomized controlled trial of LR and RFA for patients with HCC fitting the Milan criteria. Each group involved 115 patients. The prognosis was significantly superior in the LR group than the RFA group (5-year survival rate: 76 vs. 55%) [24]. Yingqiang et al. [25] stated that the collective results of their meta-analysis revealed no significant variances between the LR and RFA groups in survival rates at first and second years and in recurrence rates at first year after management of small HCC meeting the Milan criteria. They also found that the LR group had lower rates of recurrence at 3 and 5 years and higher rates of complication in comparison with the RFA group [25]. The previous findings go with our results as we reported in ablation group the recurrence rates too increased in the second and third years (80%) compared with 20% in the first year.

Conclusion

Percutaneous RFA provides a novel treatment technique for small HCC as it shows survival and tumor relapse rates comparable to LR. Because RFA is minimally invasive, less expensive, simple, harmless, accompanied with shorter hospital stay, and more economical, this technique can be considered as a first-line treatment for small HCCs. However, more studies are needed to compare the long-term outcome of LR and RFA.

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Conflicts of interest

There are no conflicts of interest.

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