

Sonographically Guided Radiofrequency Ablation of Subcapsular Hepatocellular Carcinoma

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Abstract

Background: Radiofrequency ablation is an important and ideal treatment for hepatocellular carcinoma. However; subcapsular HCC carcinoma need special care to be treated by radiofrequency ablation.

Objective: To evaluate the safety and effectiveness of percutaneous radiofrequency ablation (RFA) of subcapsular hepatocellular carcinoma (HCC).

Patients and Methods: We performed a retrospective analysis of 50 patients who underwent percutaneous ultrasound-guided RFA for treatment of HCC in Sohag University Hospital from May 2008 to April 2014. All lesions are subcapsular HCC (less than one cm from the capsule). All patients underwent contrast enhanced computed tomography imaging of the liver during follow-up and the treatment effectiveness and safety were evaluated. Incomplete ablation, recurrence, complications, and mortality were reported.

Results: Complete ablation was achieved in 45 out of 50 patients. Four patients were referred to chemo-embolization treatment. The 5th patient was lost to follow-up. Five major complications occurred in our series, namely sub-capsular hematoma (in 2 patients), pleural effusion (in 2 patients), transient ascites (in 1 patient), portal vein branch thrombosis (in 1 patient) and needle track tumour seeding (in 1 patient). No death was reported in our study.

Conclusion: Subcapsular HCC carcinoma can be treated safely and effectively by RFA using cautious techniques by experienced operators to prevent complications.

Key Words: *Radiofrequency ablation – Hepatocellular carcinoma – left lobe.*

Introduction

HEPATOCELLULAR Carcinoma (HCC) is worldwide common cancer after liver cirrhosis. HCC and cirrhosis is a common sequel of viral C hepatitis which is endemic in Egypt [1]. Ideally; HCC carcinoma is treated by surgery when there is no contraindication to do [2]. However; in presence of liver cirrhosis with disturbed liver functions

and other contraindications to surgery; there is a strength need to other curative treatment [2]. Radiofrequency ablation is a non-invasive and valid technique to treat HCC [3]. Subcapsular HCC is an important entity because it is commonly encountered. There is controversy about treating subcapsular HCC. The risk of subcapsular location of HCC seedling that may abut a hollow organ or the diaphragm. The inability to thermo coagulate the needle track after RF ablation of some subcapsular nodules may be associated with a risk of tumor seeding [3]. Thoracic and diaphragmatic complications may be result from RFA of tumors abutting the diaphragm [5,6]. The thermal injury that results from treating lesions adjacent to hollow viscera may cause gastrointestinal perforation. So, the lesion adjacent to the gastrointestinal tract was listed as a contraindication of RF ablation [7].

Even if thermal ablation is performed on tumor in such locations, the ablation time is shortened to avoid injury on the gastrointestinal tract, leaving incomplete ablation in the margin of the tumors [5].

There were many studies that reported it as high risk for complications but other series reported low complications rate. On the basis of different results and opinions about the safety and effectiveness of RFA of subcapsular HCC; we introduce our study to further investigate the subject.

Patients and Methods

From May 2008 to April 2014; we retrospectively analyzed our medical data records for patients who were undergone RFA in Sohag University Hospital

Abbreviations:

RFA : Radiofrequency ablation.
HCC : Hepatocellular carcinoma.
US : Ultrasonography.
CT : Computed tomography.

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after approval of our institutional committee and written informed consent from the patients. We found 50 patients had subcapsular HCC treated by RFA and included in our study. They were 39 males and 11 females with age range of 25-75 years; mean age is 47.3 years. All patients are cirrhotic (Child-Pugh class A are 45 cases and B 5 cases. HCC diagnosis was based tri-phasic computed tomography criteria (in 30 patients) and sonographically guided biopsy (in 20 patients) (Table 1).

Inclusion criteria are; single sub-capsular lesion less than 1cm from the liver capsule; tumour size less than 5cm in diameter, no portal or vascular invasion adjacent to the tumor. All patients are not candidates for surgery because of cirrhosis and unsuitable liver function or refusal of the patients to surgery. Patients were not candidates for RF treatment in cases of extra hepatic metastasis, severe liver dysfunction (Child-Pugh class C), or significantly abnormal coagulation test results (prothrombin activity <40%, platelet count <50 x 10⁹/L).

All patients are examined before the RFA by gray-scale and color Doppler ultrasound (US) examination, by using 3.5-MHz probes (Siemens G50 Ultrasound, Germany), as well as non enhanced and dual-phase contrast material-enhanced computed tomography (CT) using Multislice CT unit, a GE Light Speed Ultra (General Electric Healthcare; Milwaukee, WI). The first non-enhanced scanning over the entire liver with 8-mm collimation, a pitch of 1.5, and reconstructions every 8mm was followed by two contrast material-enhanced passes with 5-mm collimation, a pitch of 1.5, and reconstructions every 5mm for 20 seconds during the arterial phase and for 60 seconds during the portal venous phase of the intravenous injection of iodinated contrast medium. A 170-mL volume of the contrast medium (iohexol, Omnipaque [300mg of iodine per milliliter]; Amersham, Cork, Ireland) was systematically injected, at a rate of 5mL/min, through an 18-gauge catheter inserted into a forearm vein. All patients underwent the following laboratory tests before RFA: Complete blood count, serum aspartate aminotransferase, serum alanine aminotransferase, serum total bilirubin, serum albumin, blood urea nitrogen, serum creatinine, prothrombin time, hepatitis B surface antigen and hepatitis C antibody, and serum levels of alpha-fetoprotein. All laboratory tests were performed within 48 hours before RFA procedure.

Technique of RFA:

RFA was done with a percutaneously by using 3.5-MHz probes for real-time US guidance with

(Siemens G50 Ultrasound, Germany). All procedures were performed under strict aseptic conditions. General anaesthesia with tracheal intubation and assisted ventilation was used. The anaesthetic protocol was 0.1-2 µg/kg intravenous injections of sufentanil (Sufenta; Janssen-Cilag, Issy-les-Moulineaux, France), 1.5-2.5mg/kg of propofol (Diprivan; AstraZeneca, Rueil-Malmaison, France). Local anesthesia is used in unsuitable patients for general anesthesia. For percutaneous RFA, patients were treated using the RITA 1500 generator (RITA Medical Systems Inc., Mountain View, CA, USA). This system consists of a generator that supplied up to 150W of power and a multitined expandable electrode (Star Burst XL, RITA). The multitined expandable electrode consisted of a 15-gauge insulated cannula, 15 to 25cm in length that contains nine individual electrode tines deployed in situ after ultrasound-guided placement of the needle electrode into the liver tumour. We used indirect puncture if possible by pass through non-tumorous normal liver tissue. Depending on tumour size and location, a treatment plan was tailored that consisted of a mathematical protocol, an individualized protocol, and adjunctive measures. The goal to achieve complete necrosis of the tumour was to ablate a peripheral margin of 0.5-1 cm of normal hepatic tissue surrounding the tumour as well as the entire tumour itself so; multiple overlapping ablations techniques was used whenever necessary accordingly to the volume of the tumour and to the spread of hyperechogenic area induced by RF energy deposition during the procedure. Ablation of the used tract is done to thermo-coagulate it and prevent tumour seeding.

Follow-up of the patients after RFA procedure:

The patients were closely monitored, 1-2 hours to detect any bleeding in the liver or the peritoneal cavity. All patients stayed in the hospital overnight, and any adverse event was evaluated and reported. Patients discharged from the hospital, and were followed at the outpatient clinic with physical examination and laboratory tests at one week, one month, and then three-month intervals thereafter. Contrast enhanced CT was done by the same criteria described before. Evaluation of the treatment was assessed 1 month after ablation. The ablation was considered as complete on the basis of all of the following findings: (A) No contrast enhancement was detected within or around the tumour, (B) The margins of the ablation zone were clear and smooth, and (C) The ablation zone extended beyond the tumour borders [8].

Complications and tumor progression or seeding are reported.

Results

Fifty patients underwent sonographically guided percutaneous RFA for subcapsular HCC Figs. (1-8). Of patients with subcapsular HCC; 23 of them were near the diaphragm, 22 were near the body wall and 5 of them were near the GIT organ. The mean treatment session was 1.6/lesion. The RFA rate was complete by one session in 38 patients in one session and also completed in the second session in other 7 patients (45 out of 50 patients; 90%). Four of the five patients treated by chemo-embolization and the fifth patient has dome HCC lost to follow-up. A nodule (3cm in diameter) in a patient who failed to RFA compressed the colon. To avoid the colon injury, we infused 1000mL of 5% dextrose in water solution (mean volume, 550ml) into the peritoneal space, until the tumor was well visualized and the path for the radiofrequency electrode was fully developed.

No patient died within one month after percutaneous RFA with a mortality of 0%. The complications of percutaneous RFA are shown in (Table 2). Fever and pain were frequently encountered in our patients due to procedure technique.

In RFA for 50 HCC, 5 major complications were occurred in 7 patients (7/50, 14%) (Table 2). Subcapsular hematoma has developed in 2 patients. Pleural effusion has reported in 2 patients. Transient ascites has occurred in 1 patient. Portal vein branch thrombosis was seen in 1 patient. Tumor seeding occurred in 1 patient. Patients with subcapsular hematoma have stable vitals signs and hematocrits require no intervention except one patient previously treated with anticoagulant who required a transfusion of fresh frozen plasma and blood. Transient ascites were improved spontaneously. Total re-canalization of portal vein thrombosis was obtained after anticoagulant therapy.

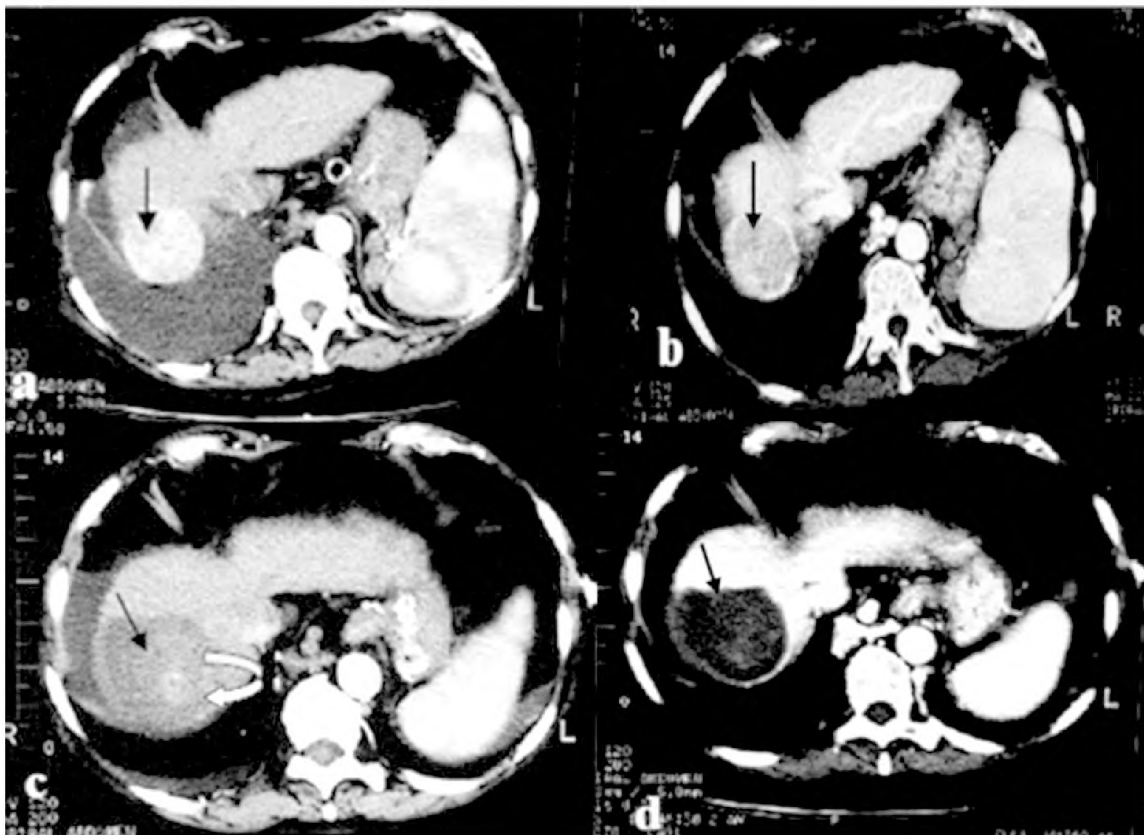


Fig. (1): A 55 year old man with HCC successfully treated with radiofrequency:

- A- Arterial phase CT image depicts 5cm right lobe subcapsular HCC (arrow). The mass shows outward bulge.
- B- Portal venous phase CT image shows tumour washout of contrast characteristic of HCC (arrow). Using 3-needle electrodes, two ablations were performed. The deep portion of the mass was treated first and then the exophytic portion.
- C- Arterial phase CT scan image obtained after 1 month after RF ablation shows an ablated lesion (arrow) with no contrast enhancement, indicating complete necrosis. Minimally hyperdense foci (curved arrow) within the ablated area represent hemorrhage.
- D- Portal dominant phase CT image shows no enhancement (arrow).

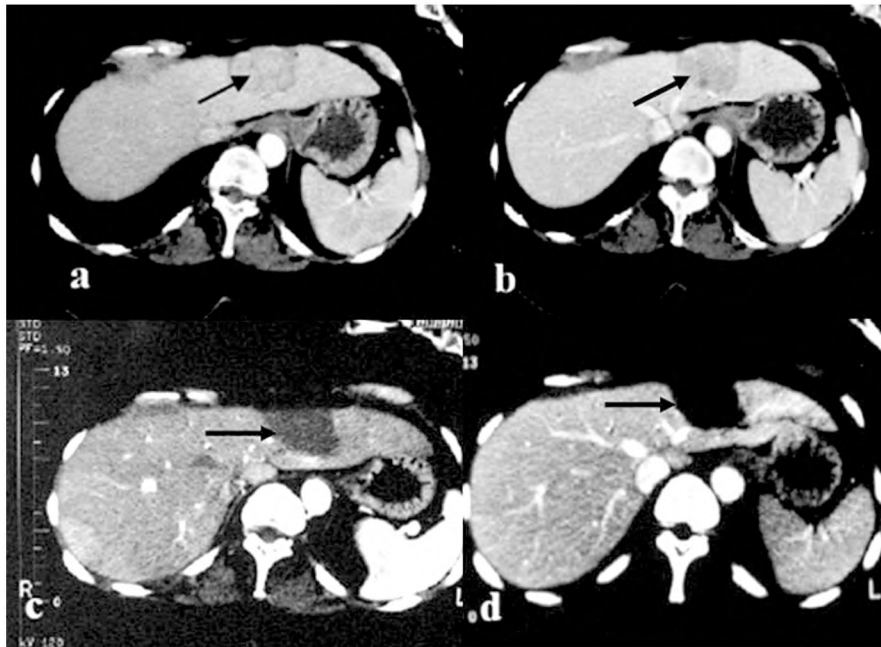


Fig (2): A 51 year old man with HCC successfully treated with radiofrequency:

- A- Arterial phase CT image before treatment shows a subcapsular tumour mass (arrow) in segment II of the left hepatic lobe with enhancement.
- B- Portal venous phase CT image shows tumour washout of contrast characteristic of HCC (arrow). Using 3-needle electrodes, the tumour was ablated under US guidance.
- C,D- Arterial and venous phases CT scan images obtained 1 month after RF ablation shows an ablated lesion (arrows) with no contrast enhancement, indicating complete necrosis. Note this area is bigger than the original tumour and includes a cuff of normal liver tissue, indicating complete ablation.

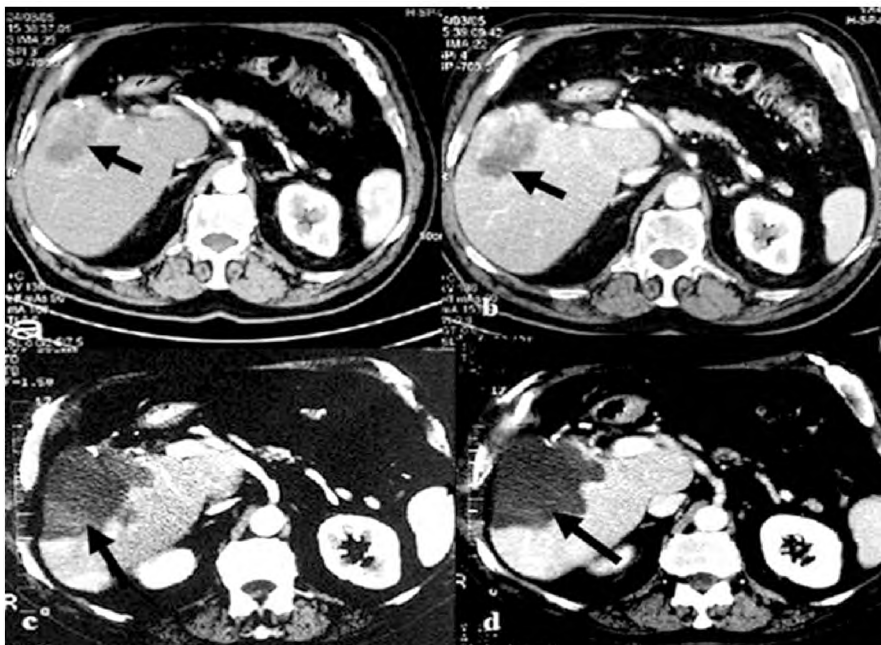


Fig. (3): A 65 year old man with HCC successfully treated with radiofrequency:

- A- Arterial phase CT image depicts 8.5cm HCC at the subcapsular region of segment V at segment V. The mass abuts the colon.
- B- Portal venous phase CT image shows tumour washout of contrast characteristic of HCC (arrow).
- C- Arterial phase CT scan image obtained after 1 month after RF ablation shows un-enhanced low attenuation ablated zone (arrow). Findings indicate technical success. Also; normal appearance of the colon adjacent to the ablated zone is noted.
- D- Portal dominant phase CT image shows no enhancement (arrow).

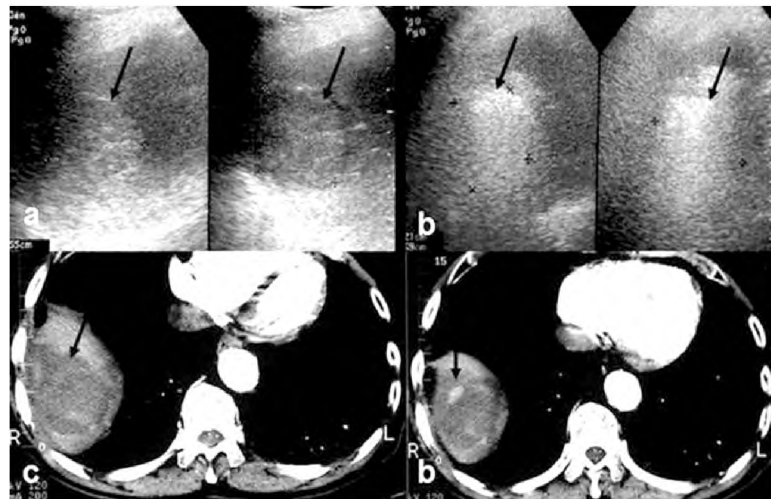


Fig. (4): A 68 year old man with 6.5cm HCC incompletely ablated after one radiofrequency procedure.
A- US transverse (on left) and longitudinal (on right) views before treatment,
B- US transverse (on left) and longitudinal (on right) views just after the end of RF procedure.
C- CT image at arterial phase performed 1 month after RF ablation procedure shows tumour almost completely ablated.
D- Few cm above c., CT image at arterial phase shows persistent of viable tumour (arrow) requiring complementary additional RF procedure.

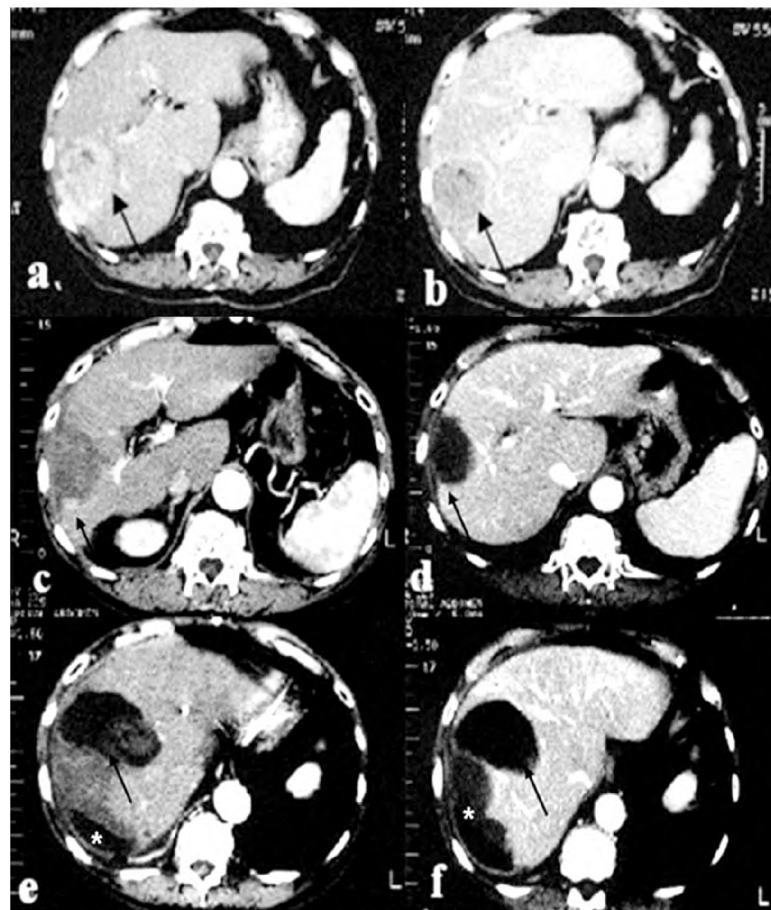


Fig. (5): A 61 year old man with HCC successfully treated with two sessions of RFA.
A- Arterial phase CT image depicts right lobe subcapsular HCC (arrow).
B- Portal venous phase CT image shows tumour washout of contrast characteristic of HCC (arrow).
C- Arterial phase CT scan image obtained after 1 month after RF ablation shows an ablated lesion but with enhanced peripheral lesion (arrow).
D- Portal dominant phase CT image shows washout of the peripheral lesion (arrow).
E- CT image obtained after one month of second session of ablation shows successful ablation with extensive ablated margin (arrow) up to the crura of the right diaphragm. Right pleural effusion is noted (*).
F- Portal dominant phase CT image shows the same findings as in E.

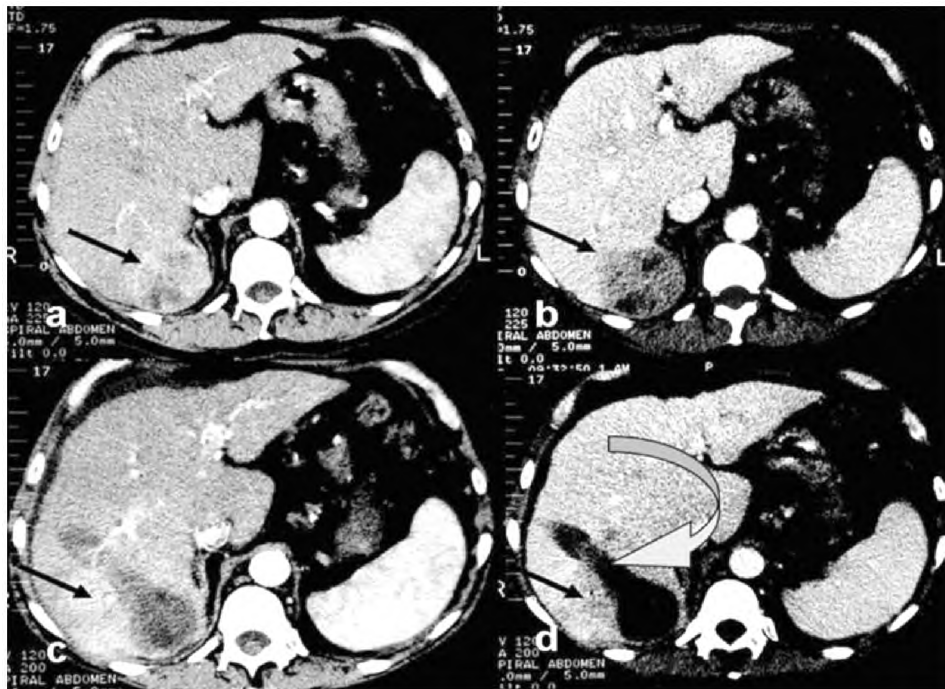


Fig. (6): A 55 year old man with subcapsular HCC unsuccessfully treated with radiofrequency.

A- CT image at the arterial phase shows infiltrative pattern of the anterior part of the tumour (arrow).

B- CT image at the portal phase confirming the infiltrative pattern of the tumour (arrow).

C- CT image at the arterial phase performed 1 month after RF ablation procedure shows active tumour growing from infiltrative part of the initial tumour (arrow).

D- CT image at portal phase performed 1 month after RF ablation procedure shows contrast medium washout consistent with viable tumour (arrow). Note the ablation tract (curved arrow).



Fig. (7): A 62 year old man with subcapsular HCC successfully treated with radiofrequency

A- CT image at arterial phase shows densely enhanced lesion (arrow).

B- US transverse images at the beginning of RF energy deposition showing the lesion (arrows).

C- US transverse (on the left) and longitudinal (on the right) images at the end of RF energy deposition showing the hyperechoic lesion region (arrows).

D- CT image at arterial phase performed 1 month after RF ablation procedure showing completely ablated lesion (arrow).

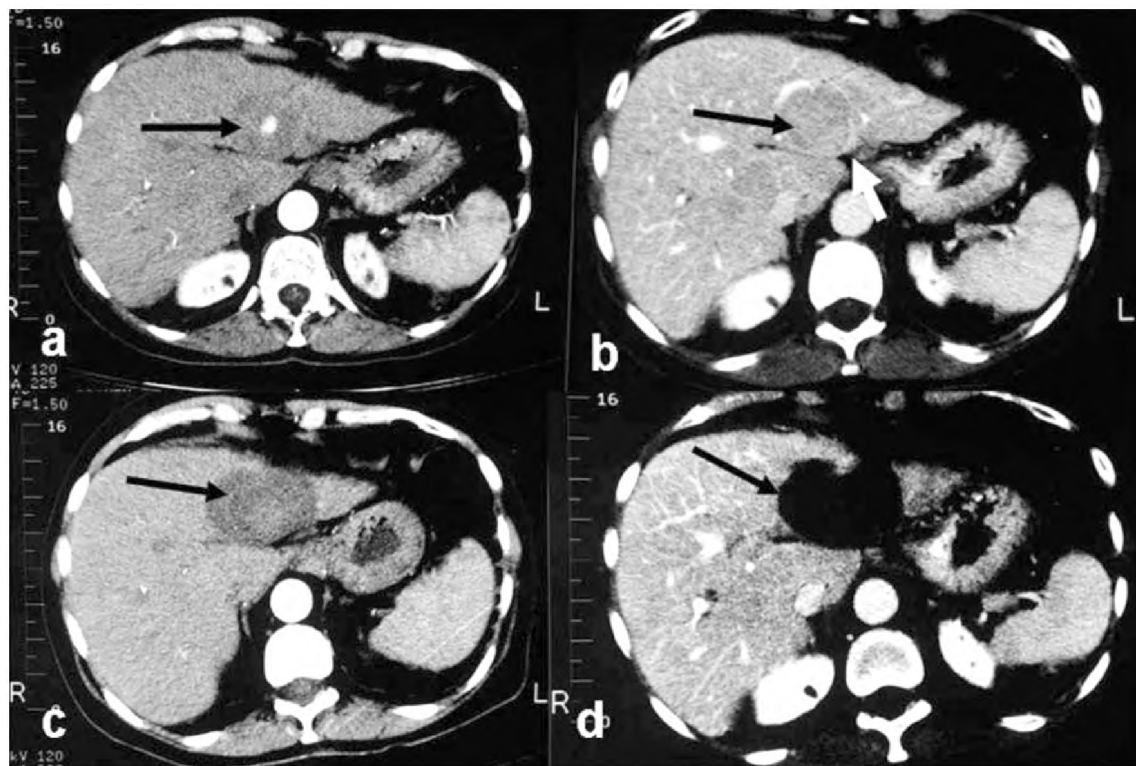


Fig. (8): A 48 year old man with HCC successfully treated with radiofrequency:

- A- Arterial phase CT image depicts left lobe HCC (arrow) with central arterial enhancement.
- B- Portal venous phase CT image shows tumour washout of contrast characteristic of HCC (black arrow). White arrow denoting that the tumour abutting the capsule US-guided RFA ablation was done.
- C- Arterial phase CT scan image obtained after 1 month after RF ablation shows an ablated lesion (arrow) with no contrast enhancement, indicating complete ablation.
- D- Portal dominant phase CT image shows the ablated region (arrow) is bigger than the lesion. Adjacent pylorus is noted adjacent to the ablated area.

Table (1): Baseline characteristics of patients in the study.

Characteristic	In 50 subcapsular HCC
Age/mean	25-75 (74.3) years
Male	39
Female	11
Child-Pugh A	45
Child-Pugh B	5
HCC proved by CT	30
HCC proved by biopsy	20

Table (2): Major complications observed in 50 patients.

Complication	Number of patients
Subcapsular hematoma	2
Pleural effusion	2
Transient ascites	1
Portal vein thrombosis	1
Tumour seeding	1

Discussion

HCC carcinoma is a big problem in Egypt [1] due to prevalence of hepatitis C with its sequelae of liver cirrhosis and HCC. Resectable HCC carcinoma with good general condition of the patient is better to be treated by surgery [2]. However many HCC are not candidates for surgery and may be because of general non-well being of the patient or other causes. Because the 5 years mortality rates of non-treated HCC is very high; alternative treatment to surgery is very necessary [9]. RFA is min-

imally invasive curative technique in comparison to surgery. Sonographically guided radiofrequency ablation is widely used for treatment of HCC carcinoma especially noncapsular lesions. There is strong debate about treatment of subcapsular HCC. Some studies report a high incidence of needle track seeding and increased complication and local recurrence rates after RFA of subcapsular HCC [10-13]. Llovet et al., [10] reported a high incidence (12.5%) of tumor seeding in the needle track among thirty-two patients who underwent RFA for HCCs. All four cases occurred in patients

with subcapsular HCC, which was identified to be a significant risk factor for needle track seeding. Another group reported three major treatment-related complications after RFA for subcapsular HCC, namely, subcapsular hematoma, sustained severe pain, and peritoneal dissemination [11]. This group of authors also suggested that subcapsular HCC has to be excluded from RFA. A more recent study by a Japanese group reported that patients with subcapsular HCC had a significantly higher incidence of local recurrence after percutaneous RFA than those with non-subcapsular HCC. Thus, the authors suggested that subcapsular HCCs may be less suitable for RFA [12].

On the other hand, other study do not exclude subcapsular HCC from RFA [14]. Poon et al., [15] recently reported that the results for radiofrequency ablation of subcapsular HCC using internally cooled electrodes were comparable in local tumor progression rate and complication rate to the results for radiofrequency ablation of nonsubcapsular HCC.

This controversy in opinions about percutaneous RFA of subcapsular HCC may be multi-factorial. Direct puncture of tumour, insufficient ablation, inexperienced operators and inefficient machines may be some factors that decrease the safety and effectiveness of RFA.

In our study, we successfully ablated 45 HCC of 50 lesions (90%). This efficacy of RFA is comparable with other published reports [3,6]. The complications rate in our study is to somewhat comparable to other studies [16-19] of RFA of subcapsular HCC. As regards minor complications; pain and fever are frequently faced in RFA [9] and are due to technical and procedural factors. They are reported in all literatures and were relieved by analgesic antipyretic on close follow-up. Pleural effusion is commonly occurred due to sympathetic effusion of nearby irritated pleural layer overlying the diaphragm. It is spontaneously improved on close follow-up. It is reported in most of the recent studies. Sub-capsular hematoma is the most reported major complication in most of the reported series. Most of the hematoma relived on follow-up period. Tumour seeding is the most risky outcome of RFA. This complication occurred in one patient in our study. Mostly due to inefficient thermo-coagulation of the needle track for RFA. Tumour seeding was reported in many series and occurred with higher incidence than ours [3,10]. No treatment related deaths had occurred in our study (mortality=0%).

Our study had some limitations. It contains only 50 patients and they somewhat small sample

of patients. Patient selection is another limitation. We concentrated upon sub-capsular lesions only.

Conclusion:

RFA is a good minimally invasive technique for curative treatment of sub-capsular HCC with usage of good patient selection; experienced operators, good machines and use of suitable techniques especially indirect needle puncture through normal liver tissue and subsequent thermo-coagulation of the needle track.

Conflict of interest:

We have no conflict of interest to declare.

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الملخص العربي

وكان الهدف من الدراسة تقييم أمان وتأثير الكي بالتردد الحراري بإرشاد الموجات فوق الصوتية على الأورام السرطانية تحت قشرية.

وقد أشتملت الدراسة على ٥٠ مريض ثبت إصابتهم بأورام الكبد السرطانية وقرر لهم العلاج بالكي بواسطة التردد الحراري في مستشفيات جامعة سوهاج في الفترة ما بين مايو ٢٠٠٨ وأبريل ٢٠١٤. وكانت كل الأورام تقع تحت القشرة الكبدية، وقد تم متابعة الحالات بإجراء فحص بالأشعة المقطعية بالصبغة لتقييم تأثير ومضاعفات الكي بالتردد الحراري.

وقد تم عمل كي كامل ل ٥ حالة وتم إحالة ٤ حالات للحقن الكيماوي للشريان الكبدي، وقد حدث ٥ مضاعفات كبيرة للحالات وهي تجمع دموي تحت القشرة في حالتين، وإرتشاح بلوري في حالتين، وإستسقاء مؤقت في حالة واحدة وجلطة في الوريد البابي في حالة واحدة وإستزراع ورمي في مسار الإبرة في حالة واحدة. ولم يسجل أي حالات وفيات.

وقد أستخلص من هذه الدراسة انه يمكن علاج أورام الكبد السرطانية تحت قشرية بالكي بالتردد الحراري بأمان وذلك بإستعمال طرق حذرة وأيدي ماهرة لمنع حدوث مضاعفات.