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ORIGINAL ARTICLE

Hepatocellular Carcinoma in Egypt: A Comprehensive Treatment Modalities

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Abstract

Background: **Hepatocellular carcinoma (HCC) is the fifth most common neoplasm in the world and the third most common cause of cancer death worldwide. HCC is responsible for more than one million deaths annually worldwide, representing 10 % of all deaths from cancer.**

Objective: **To determine the different survival rates of HCC after different modalities of management: radiofrequency ablation (RFA), transarterial chemoembolization, liver resection and living donor liver transplantation.**

Patients and methods: **This study was conducted on 50 patients having HCC during the period from March 2014 to May 2017. They were classified according to their ages into three groups, the first one included eight (16 %) patients above 60 years, 38 (76 %) patients between 50 and 60 years in the second group, and four (8 %) patients below 50 years in the last group.**

Results: **Of the 50 treated patients, 20 HCC nodules were treated in 20 sessions, 10 patients were with a single session, and five patients with two sessions. In these 10 patients who subjected to RFA was apparent. This response continued with follow up, as patients mass and alpha fetoprotein level decreased with time. In patients who did not respond well, we did the second ablation. Four of those five patients, showed improvement and 18 sessions of transarterial chemoembolization were done for these 10 patients. Two patients had taken two sessions, while three patients received three sessions. Five patients received only one session as there was no improvement after the session diagnosed by computed tomography. One patient developed recurrence after 6 months and two patients within 2 years.**

Conclusion: **The utilization of RFA as a therapeutic intervention has demonstrated noteworthy long-term survival outcomes that are equal to those achieved with surgical resection in the management of small HCC.**

Keywords: Hepatocellular carcinoma, Radiofrequency ablation, Liver transplantation

1. Introduction

Hepatocellular carcinoma (HCC) ranks as the fifth most prevalent neoplasm globally and stands as the third leading cause of cancer-related mortality on a global scale. HCC is accountable for a global annual mortality rate over one million individuals, constituting ~10 % of all cancer-related deaths.[1]

The difficulties in treatment of this cancer, and reason for the high mortality, result from three factors. First, this cancer is usually associated with cirrhosis, which both limits the treatment options and increases the morbidity of any given therapy. Second, HCC is usually asymptomatic at early stages, and has a great propensity for intravascular or intrabiliary extension, even when the primary tumor is small. As a result, HCC is usually at an

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advanced stage when discovered. Third, this tumor has been resistant to most conventional forms of cytotoxic chemotherapy.[2]

Because the liver is relatively hidden behind the right costal cartilages, tumors have to reach substantial size before they are palpable. Furthermore, the large functional reserve of the liver masks any small impairment produced by local parenchymal disturbances. Small tumors are therefore most often asymptomatic, and are usually discovered during screening programs or incidentally during imaging performed for other abdominal conditions.[3]

The present study aimed to determine the different survival rates of HCC after different modalities of management: radiofrequency ablation (RFA), transarterial chemoembolization (TACE), liver resection and living donor liver transplantation (LDLT).

2. Patients and methods

This study was approved by the Medical Ethics Committee of Al-Azhar University No 1132 for the year 2014.

This study was conducted upon 50 patients with HCC treated from March 2014 to May 2017 with exclusion of patients with extrahepatic metastasis.

Our 50 patients were divided into two equal groups:

Group A (nonsurgical management) were subdivided into subgroup 1 where RFA was done in 15 (30 %) patients and subgroup 2 where TACE was done in 10 (20 %) patients.

Group B (surgical management) were subdivided into subgroup 3 where hepatic resection was done in 15 (30 %) patients and subgroup 4 where LDLT was done in 10 (20 %) patients.

2.1. Inclusion criteria for radiofrequency ablation

Patients Child's A or Child's B class. Presence of a single hepatic lesion or multiple (up to 3) lesions less than 3 cm each. The lesions were away from important structures (e.g. hepatic hilum). The lesions were a site accessible by ultrasound (US) and/or computed tomography (CT). Prothrombin time not less than 50 %. Platelet count not was less than 70.000.

Before the initiation of the experiment, all participants granted their informed permission throughout the registration process following a thorough elucidation of the nature of the procedure.

The effectiveness of RFA was evaluated through the utilization of spiral CT during a timeframe of 2–5 weeks postprocedure, as well as by the application of alpha fetoprotein (AFP) assays within a timeframe of 10–15 days postprocedure.

The identification of distinct, nonenhancing tissue in images acquired during both precontrast and postcontrast phases of CT with contrast administration suggested the occurrence of tissue necrosis. The nonenhancing areas exhibited maximum diameters that were equivalent to or greater than the maximum diameters of the HCC nodules before treatment.

A second RF procedure was planned for one patient who did not show complete response after the first procedure.

The long-term follow-up assessments consisted of regular monitoring using serum AFP assay and US every 3 months, as well as spiral CT every 3 months during the first year and every 6 months thereafter for a duration of up to 2 years.

2.2. Inclusion criteria for transarterial chemoembolization

Patients with Child B. Unresectable tumor. Tumor is responsive to chemoembolization. No major contraindications to angiography. Satisfactory liver function (normal alkaline phosphatase (AP) and aspartate transaminase (AST) levels). Serum bilirubin level less than 5 mg/dl. Serum creatinine level less than 2 mg/dl. Complete blood count (CBC) (white blood cell count >2.5, platelet count >60 or hemoglobin level >8 g/dl).

Noncontrast CT scan was done on the second day after the procedure to assess postembolization lipiodol distribution. Follow-up US and liver function assessment were done after 3 weeks. Precontrast and postcontrast CT scan was done after 6 weeks to determine the residual lipiodol distribution, residual enhancement within the lesion to detect development of recent tumor nodule, and to plan the next chemoembolization session.

We preformed chemoembolization based on tumor response as assessed by US and CT. If lipiodol uptake was complete or incomplete but involving more than 50 % of the tumor volume, the patient was followed up closely using ultrasonography every 4 weeks and CT scan every 3 months. However, if lipiodol uptake was less than 50 % then another session of chemoembolization was carried out after 5–8 weeks.

Regarding this fact, we had done two sessions in three patients, three sessions in four patients, and four sessions in four patients.

Subgroup 3 (liver resection): 15 (30 %) patients were managed by liver resection, nine (18 %) by

right hepatectomy, two (4 %) by left hepatectomy, and four (8 %) by nonanatomical resection.

2.3. Inclusion criteria for liver resection

Absence of extrahepatic metastasis. Patients with class A. Single mass or two to three masses less than 3 cm. Anatomically resectable unilobar or bilobar disease. Adequate liver function reserve.

CT volumetry was done preoperative to measure the adequate remaining liver volume. In our work up to 40 % was considered adequate as our patients were all cirrhotic.

2.4. Early postoperative (2–4 weeks)

Complete laboratory investigations were done including: CBC, liver function test (LFT), kidney function test (KFT), and bleeding profile. Clinical and radiological evaluation were done by abdominal US for detection of early postoperative complication. CT was done if needed.

2.5. Long-term follow up

The data of the patients collected at 3, 6, 12, 18 months and 2 years including: clinical follow up, laboratory results (CBC, LFT, KFT, and bleeding profile), radiological changes (US), and level of AFP.

2.6. Inclusion criteria for living donor liver transplantation

Patients with Child class C. Single mass less than 5 cm or two to three masses less than 3 cm. After fulfillment of these investigations there is informed special consent for each of these patients; they had to sign it.

2.7. Statistical analysis

Data were presented in the form of number and percent for categorical data and for numerical data number and mean are obtained.

3. Results

The patients were categorized into two distinct groups based on the type of surgery they underwent. Subsequently, within each group, further subdivisions were made based on the specific operations performed, as outlined in Table 1.

Age and sex distribution of the two groups were shown in Table 2.

Patients were classified according to child Pugh into three classes A, B, C as in Table 3.

Table 1. Groups, subgroups, number, and percentage of the studied two groups: surgical and nonsurgical.

Number	Nonsurgical group		Surgical group	
	Subgroup 1: RFA	Subgroup 2: TACE	Subgroup 3: liver resection	Subgroup 4: LDLT
n (%)	15 (30)	10 (20)	15 (30)	10 (20)
Total	25 (50)		25 (50)	

LDLT, living donor liver transplantation; RFA, radiofrequency ablation; TACE, transarterial chemoembolization.

Table 2. Age and sex distribution of the studied two groups: surgical and nonsurgical.

Variables	Nonsurgical [*n* (%)]		Surgical [*n* (%)]		Total
	Subgroup 1	Subgroup 2	Subgroup 3	Subgroup 4	
Age					
<50	1 (2)	0	2 (4)	1 (2)	4 (8)
50–60	13 (26)	5 (10)	11 (22)	9 (18)	38 (76)
>60	1 (2)	5 (10)	2 (4)	0	8 (16)
Sex					
Male	13 (26)	9 (18)	11 (22)	9 (18)	42 (84)
Female	2 (4)	1 (2)	4 (8)	1 (2)	8 (16)

Table 3. Classification of patients according to Child Pugh.

Number of patients	Nonsurgical [*n* (%)]		Surgical [*n* (%)]	
	Subgroup 1	Subgroup 2	Subgroup 3	Subgroup 4
Class A	5 (10)	0	15 (30)	0
Class B	10 (20)	10 (20)	0	0
Class C	0	0	0	10 (20)
Total	15	10	15	10

Table 4. Laboratory investigations.

Variables	Nonsurgical				Surgical			
	Group 1	Mean	Group 2	Mean	Group 3	Mean	Group 4	Mean
Serum albumin	2.6–3.5	2.98	2–3	2.53	3.4–4.6	6.26	2–2.5	2.24
Total bilirubin	0.5–2.5	1.51	1.9–2.8	2.3	0.4–1.4	0.9	2.9–4.9	4.88
INR	1–1.6	1.3	1–1.9	1.41	0.9–1.4	1.13	1.6–2.5	2.08
AFP	9–538	143.7	100–831	359.9	15–222	109.46	11–115	39.6

AFP, alpha fetoprotein; INR, International Normalized Ratio.

Table 5. Tumor size, number of masses and site.

Variables	Nonsurgical [*n* (%)]		Surgical [*n* (%)]	
	Subgroup 1	Subgroup 2	Subgroup 3	Subgroup 4
Tumor size				
£3 cm	15 (30)	0	5 (10)	4 (8)
>3 cm	0	10 (20)	10 (20)	6 (12)
Number of masses				
Single	5 (10)	0	5 (10)	6 (12)
Multiple	10 (20)	10 (20)	10 (20)	4 (8)
Site (lobe)				
Right	10	7	11	7
Left	4	2	4	1
Both	1	1	0	2

Table 6. Follow up of patients with two settings of ablation.

Cases	Pre-ablation		Post-ablation					
			3 months		6 months		1 year	
	Mass size (in cm)	AFP level	Mass size	AFP level	Mass size	AFP level	Mass size	AFP level
Mean ± SD	2.94 ± 0.08	332 ± 176	2.6 ± 0.13	242.8 ± 122.6	1.98 ± 0.3	76 ± 45.7	0.7 ± 0.6	35 ± 18.4

AFP, alpha fetoprotein.

Patient's laboratory investigations include serum albumin, total bilirubin, International Normalized Ratio (INR) and AFP as shown in Table 4.

In Table 5 tumor size, number of masses, and site of tumor were documented.

Pre-RFA ablation mass size and AFP then follow up of patients with two settings of ablation, regarding size of lesions and AFP level after 3, 6, and 12 months as shown in Table 6.

Pre-RFA ablation mass size and AFP then follow up of patients with single ablation, regarding size of lesions and AFP level after 3, 6, and 12 months as shown in Table 7.

Table 8. Site of injection, number of sessions, and degree of response to management.

	Site of injection	Number of sessions	Degree of response
Case 1	Proper	3	Partial
Case 2	Right	3	Partial
Case 3	Left	2	Complete
Case 4	Right	1	Mild
Case 5	Right	3	Partial
Case 6	Right	1	No response
Case 7	Left	2	Complete
Case 8	Right	1	Mild
Case 9	Proper	1	No response
Case 10	Right	1	Mild

Table 7. Follow up of patients with single ablation.

Cases	Pre-ablation		Post-ablation					
			3 months		6 months		1 year	
	Mass size (in cm)	AFP level	Mass size	AFP level	Mass size	AFP level	Mass size	AFP level
Mean ± SD	2.52 ± 0.3	50.6 ± 39	1.58 ± 0.5	29.4 ± 26	0.75 ± 0.4	15 ± 7.1	0.5 ± 0.1	5.7 ± 4.3

AFP, alpha fetoprotein.

Table 9. Mass size, type of liver resection, morbidity, and mortality.

	Mass size	Type of res.	Active cirrhosis	Degree of differentiation	Vascular invasion	Hepatitis virus	Blood transfusion	Morbidity	Mortality
Case 1	2.5	Atypical	No	Well	No	HCV	No	Ascitis	
Case 2	4.5	Left	No	Moderate	No	HCV	Yes	Ascitis	
Case 3	5	Right	No	Moderate	No	HCV	Yes		Intraoperative bleeding
Case 4	3	Atypical	No	Moderate	No	HCV	No		
Case 5	6	Right	No	Moderate	No	HCV	Yes	Pleural effusion	LCF
Case 6	5.5	Right	Yes	Poor	Yes	HCV	Yes	Recurrence and pleural effusion	Metastasis
Case 7	4.5	Right	No	Moderate	No	HCV	Yes	Intraoperative bleeding	
Case 8	2.8	Atypical	No	Well	No	HCV	No		
Case 9	6	Right	Yes	Poor	Yes	HCV HBV	Yes	Recurrence	Metastasis
Case 10	3	Atypical	No	Well	No	HCV	No		
Case 11	5.5	Right	No	Moderate	No	HCV	Yes	Bile leak and recurrence	
Case 12	3.5	Right	Yes	Poor	No	HCV HBV	Yes		Acute LCF
Case 13	5	Right	No	Moderate	No	HCV	Yes	Acute LCF	
Case 14	3	Left	No	Moderate	No	HCV	Yes	Wound infection	
Case 15	4.5	Right	No	Poor	No	HCV	Yes	Bile leak and biloma	LCF

Table 10. Mortality in liver resection and living donor liver transplantation groups.

	Period of survival	Number of lost patients	Mortality %
Liver resection group	0–6 months	2	13.3
	6–24 months	4	26.6
LDLT group	0–6 months	2	20
	6–24 months	2	40

LDLT, living donor liver transplantation.

Site of injection, number of sessions and degree of response to management were documented in Table 8.

In liver resection group size of mass, type of resection, cirrhosis activity, degree of differentiation, vascular invasion, type of hepatitis viruses, blood transfusion, morbidity, and mortality were shown in Table 9.

Mortality after liver resection and LDLT documented in Table 10.

4. Discussion

In RFA group, five patients were Child A, while 10 patients were Child B. All patients were cirrhotic, one patient was HCV and HBV positive and the rest of patients were HCV positive alone. AFP was elevated in 66.6 %. AFP ranged from 9 to 538 ng/ml. Yang et al.[4] stated that elevated AFP was found in 54.8 %, where 20–400 ng/ml in 82, more than 400 ng/ml in 47 %, and the highest level was 9934 ng/ml.

In TACE group our patients were all with Child B. all the patients had HCV but three of them had both HBV and HCV. Child–Pugh classes were A and B in 37 instances and C in six instances by Timm et al.[5]

In study of RFA, all patients were with mass tumor less or equal to 3 cm in size. Ten patients were with single lesions while the other five patients were with two lesions. Ten patients managed with a single session and five patients with two sessions. But in Yang et al.[4] the HCCs had sizes ranging from 1.2 to 6.7 cm, with an average diameter of 3.9 ± 1.3 cm. Out of the total sample size of 226 patients, 158 individuals were diagnosed with a solitary tumor, while the remaining patients had numerous tumors ranging from 2 to 5. The cohort consisted of patients who presented with a total of 392 HCC nodules.

Eighteen sessions of TACE were done for our 10 patients. Four sessions were done in the hepatic artery proper for patients suffering from bilateral hepatic lesions, 10 sessions in the right hepatic artery and four sessions in the left hepatic artery for right-sided and left-sided hepatic tumors, respectively. So overall, two patients had taken two sessions were conducted, with three patients receiving three sessions. A total of five patients were administered a single session. A total of 102 TACE sessions were administered to 43 patients.[5] A total of 14

patients received a single session, whereas 29 patients underwent between two and eight TACE sessions. A distribution of bilobar HCC was observed in 40 % of the patient population. A total of 14 individuals presented with solitary HCC. In Kamada et al.[6] mean number of sessions was three.

For our 50 patients, major hepatic resection was performed in 11 (73.4 %) patients, of which right hepatectomy done in nine (60 %) patients and left in two (13.4 %) patients. Minor resection included four (26.6 %) patients. Carlis et al.[7] stated that, major liver resections were performed in 27 cases, segmentectomies in 90, and wedge resections in 27. In the study of Bruix et al.[8] major hepatectomy done for 42 % of patients and minor hepatectomy done in 58 % of patients. In Nuzzo et al.[9] 100 resections were done. Limited resection was performed in 15 cases, resections of one to two segments in 51, and major hepatectomies in 34. Patients in Dahiya et al.[10] underwent minor (£ 2 segments) in 259 patients and major (^{3} 3 segments) hepatectomy in 114 patients. Kang and colleagues showed that, 12.6 % of patients underwent nonanatomic resection and 82.4 % underwent anatomic resection. Anatomic resection involved right hepatectomy in 30 patients, left hepatectomy in 13, left trisegmentectomy in three, segment-ectomy in 72, and left lateral segmentectomy in 28. When we compare our result in type of resection with other studies mentioned before. We founded that they had done more limited than us. This is possibly due to their early diagnosis which enables them to work on small masses so limited resection was the result.[11]

RFA group. No treatment-related mortality was in Hosoda et al.[12] where the mortality related to RFA was zero in this series. These results are comparable to our study, as only one patient died and this was not related to RFA but from other cause (cardiac cause).

In LDLT group. Hospital mortality occurred only in two (20 %) patients due to bleeding and septicemia. Patients with intraoperative bleeding died at ICU in the same day of transplantation. While patients with septicemia died after 1 week of the transplantation day. Other causes included recurrence which caused death via progression of the disease and distant metastasis. LCF with hepatorenal failure was another cause responsible for mortality of another patient. Regarding donors there was no mortality recorded in our study.

Fourteen patients in our study showed complete response which was agreed with Chen et al.[13] when he concluded that a single session of RFA may be sufficient for most of the patients. Our results were comparable with studies that used RFA in mass less or equal to 3 cm. If we combine this issues with the good general condition of our patients; as all patients were child class A and B with good liver reserve. But we have two points to discuss; first our number was 15 patients which considered low compared with all studies mentioned here except in Herbold et al.[14] who had eight patients. The other point is following up period of the patients which was up to 5 years in Yang et al.[4] Also, there is an issue concerned in Egyptian patients; which is unavailability for follow up.

In our study in TACE group, 6 months, 1 year, and 18 months survival was 80, 50, and 20 %, respectively in TACE group. Gramenzi and colleagues the median survival duration observed in the study was 21 months. The survival rates at 1, 3, and 5 years were found to be 68, 31, and 16 %, respectively. Notably, there were significant variations in survival outcomes based on factors such as Child–Pugh class, AFP levels, as well as the size and number of nodes.[15] Survival was in first year 68 %, 2 years 37 %, and 3 years 0 % in[8] study.

In our study in liver resection group. Six-month and 18-month survival was 26.6 and 13.3 %, respectively. Regarding other survival incidence we can see in Shah et al.[16] study the 1-, 3-, and 5-year disease-free survival rates were 72, 48, and 39 %, respectively. One-, 3-, and 5-year survival rates were 85, 68, and 53 %, respectively. The study reported a median overall survival of 71 ± 11 months. Disease-free survival, on the other hand, had a range of 1–149 months, with a median of 34 months. Nuzzo et al.,[9] overall mean survival time was 41 months. The 5- and 10-year survival rates were 44 and 24 %, respectively. Taking into account the number of neoplastic nodules, the 5-year survival was 54 % for 74 patients with a single nodule and 20 % for 20 patients with 3 or more nodules.

4.1. Conclusion

The utilization of RFA as a therapeutic intervention has demonstrated noteworthy long-term survival outcomes that are equal to those achieved with surgical resection in the management of small HCC. RFA has the potential to serve as a viable initial therapeutic option for individuals diagnosed with small HCC measuring 3 cm in size.

Conflicts of interest

There are no conflicts of interest.

References

1. Pfitzmann R, Schwenger J, Rayes N. Long-term survival and predictors of relapse after liver transplantation for alcoholic liver disease. *J Liver Transpl*. 2017;13:197–205.
2. Becker G, Soezgen T, Olschewski M. Combined TACE and PEI for palliative treatment of unresectable hepatocellular carcinoma. *J Gastroenterol*. 2015;11:104–109.
3. Todo S, Furukawa H. Living donor liver transplantation for adult patients with hepatocellular carcinoma: experience in Japan. *J Ann Surg*. 2014;240:451–459.
4. Yang B, Zou J, Xia J. Risk factors for recurrence of small hepatocellular carcinoma after long-term follow-up of percutaneous radiofrequency ablation. *J Eur Radiol*. 2010;49:855–862.
5. Timm S, Sotiropoulos G, Draier M. Selective trans-arterial chemo-embolization of advanced hepatocellular carcinomas: a reasonable palliative option. *J Transplant*. 2010;40: 3179–3181.
6. Kamada K, Kitamoto M, Aikata H. Combination of transcatheter arterial chemo-embolization using cisplatin-lipiodol suspension and percutaneous ethanol injection for treatment of advanced small hepatocellular carcinoma. *J Am Surg*. 2012; 184:284–290.
7. Carlis L, Giacomoni A, Pirotta V. Treatment of HCC: the role of liver resection in the era of transplantation. *J Transplant*. 2011;33:1453–1456.
8. Bruix J, Reig M, Sherman M. Evidence-based diagnosis, staging, and treatment of patients with hepatocellular carcinoma. *Gastroenterology*. 2016;150:835–853.
9. Nuzzo G, Giuliante F, Gauzolino R. Liver resections for hepatocellular carcinoma in chronic liver disease: experience in an Italian centre. *J ESO*. 2017;33:1014–1018.
10. Dahiya D, Wu T, Lee C. Minor versus major hepatic resection for small hepatocellular carcinoma (HCC) in cirrhotic patients: a 20-year experience. *J Surg*. 2010;147:676–685.
11. Kang C, Choi G, Kim D. Revisiting the role of nonanatomic resection of small ($\leq$4 cm) and single hepatocellular carcinoma in patients with well-preserved liver function. *J Surg Res*. 2010;160:81–89.
12. Hosoda K, Yagawa A, Hanawa M. long-term follow-up after radiofrequency ablation (RFA) for small hepatocellular carcinoma (HCC). *J Hepatol*. 2010;52:S59–S69.
13. Chen M, Li J, Zheng Y. A prospective randomized trial comparing percutaneous local ablative therapy and partial hepatectomy for small hepatocellular carcinoma. *J Ann Surg*. 2016;243:321–328.
14. Herbold T, Wahba R, Bangard C, Demir M, Drebber U, Stippel DL. The laparoscopic approach for radiofrequency ablation of hepatocellular carcinoma-indication, technique and results. *Langenbeck's Arch Surg*. 2013;398: 47–53.
15. Gramenzi A, Mirici-Cappa F, Santi V. Treatments for epatocellular carcinoma in elderly patients are as effective as in younger patients: a 20-year multicentre experience. *Gut*. 2010; 59:387–396.
16. Shah S, Cleary S, Wei A. Recurrence after liver resection for hepatocellular carcinoma: risk factors, treatment, and outcomes. *J Surg*. 2017;141:330–339.