Journal of Digestive Diseases and Hepatology

Research Article

Yi M, et al. J Dig Dis Hepatol 2016: JDDH-120.

A Single Institutional Experience of Local Therapy in 1136 Patients with Hepatocellular Carcinoma Associated with Cirrhosis

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Citation: Ke Z, Li J, Zhenhao D, Ronghai H, Yi M et al. (2016). A Single Institutional Experience of Local Therapy in 1136 Patients with Hepatocellular Carcinoma Associated with Cirrhosis. J Dig Dis Hepatol 2016: JDDH-120.

Received Date: 29 November, 2016; **Accepted Date:** 15 December, 2016; **Published Date:** 22 December, 2016

Abstract

Background: Recent studies have suggested that percutaneous radiofrequency ablation (RFA) has comparable outcomes to surgical resection in early stage hepatocellular carcinoma (HCC) .This study compares the short- and long-term outcomes of RFA and surgical resection for HCC in cirrhotic patients.

Methods: Between June 2007 and June 2015, 1136 consecutive cirrhotic patients with HCC were treated with surgical resection (SR group) or RFA (RFA group).The prognoses, complications, total and tumor-free survival rates between the two treatment modalities were compared.

Results: There were no 30-day mortality in either group. Major complications occurred significantly in the SR group than in the RFA group (P = 0.001). There was no significant difference in the total survival rates of the two groups. The tumor-free survival rate in the SR group was higher than in the RFA group (P<0.05).

Conclusion: RFA appears to successfully ablate HCC in cirrhotic patients with fewer complications as compared to surgical resection. Its treatment efficacy is equivalent to that of surgical resection, but it has a shorter tumor-free survival rate.

Keywords: Hepatocellular carcinoma; Liver resection; Radiofrequency ablation; Survival rate

Introduction

Hepatocellular carcinoma is the sixth most common neoplasm and the third most frequent cause of cancer death [1].Liver transplantation, which offers the potential for complete tumor resection and replacement of the cirrhotic liver , achieves the best result but can be offered only to a few of patients because of the shortage of liver donors [2,3]. In this way, surgical resection has generally become accepted as the first treatment of choice for HCCin many medical centers[4]. Advancements in surgical equipment, instruments, and surgical skills have left no part of the liver inaccessible to surgery [5, 6].

A significant proportion of Chinese HCC patients have concomitant cirrhosis [7, 8]. The issue of preserving normal liver parenchyma during HCC resection is essential in maintaining adequate liver function, especially in cirrhotic patients.When the tumor is located deep within the liver and adjacent to main intrahepatic vessels, a large part of the liver parenchyma has to be removed. For this reason, it is critical to develop a surgical plan and avoid post-surgical liver failure [9]. RFA can destroy tumors effectively, and its efficacy is equivalent to surgical resection when limited to tumors ≤ 3cm in diameter [10,11]. Whether surgical resection or RFA is the better initial treatment for HCC has been debated extensively [4]. Between 2007 and 2015, 1136cirrhotic patients with HCC underwent surgical resection or RFA in our department. In this study, we analyzed our retrospective experience in HCC cirrhotic patients to assess the short- and long-term effects of surgical resection and RFA therapy.

Methods

Patients

A total of 1136 consecutive cirrhotic patients with HCC were treated between June 2004 and June 2012. Among them, 574 patients were treated with surgical resection and 562 patients were treated with RFA. A total of 808 cancer nodules were ablated in the RFA group. All patients were diagnosed with HCC before treatmentaccording to the guidelines used by the European Association for the Study of the Liver [12]: (a) demonstration of typical features of HCC with two imaging techniques or positive findings on one imaging study together with an alpha-fetoprotein (AFP) level of more than 400 ng/mL (n = 741) or (b) cytologic and/or histologic diagnosis of HCC (n = 395, 364 patients in the RFA group). Cirrhosis was confirmed by histology or by corroborating radiologic and laboratory parameters. Portal hypertension (PH) was diagnosed in the presence of one or more of the following conditions: esophageal-gastric varices, splenomegaly with white blood cell (WBC) count <4000/mm3 and/or platelet (PLT) count < 100,000/mm3, actual or pre-existing ascites, hepatic vein pressure gradient > 10 mmHg[13].The patients' general information is given in Table 1. This study was approved by the ethics committee of Beijing Ditan Hospital, Capital Medical University. All patients signed a written consent form and agreed that their medical information may be used in a study.

	SR group (574)	RFA group (562)	t or χ^2 value	P value	
Gender			0.666	0.414	
Male	402 (70.03%)	381 (67.79%)			
Female	172 (29.97%)	181 (32.21%)			
Age	42.1±9.6	41.2±10.0	1.5476	0.061	
Underlying cirrhosis			3.9255	0.27	
HBV	395 (68.82%)	414 (73.67%)			
HCV	96 (16.72%)	86 (15.30%)			
Alcoholic	61 (10.63%)	45 (8.01%)			
PBC	22 (3.83%)	17 (3.02%)			
AFP level (ng/ml)	441.5±169.2	425.0±210.4	1.4581	0.073	
Numbers of tumors			43.7163	<0.001	
Single	414 (72.13%)	297 (52.85%)			
Multinodular	160 (27.87%)	265 (47.15%)			
Single nodule size			135.177	<0.001	
≤3cm	93 (22.46%)	177 (59.60%)	101.2337	<0.001	
>3cm and ≤5cm	232 (56.04%)	120 (40.40%)	16.9108	<0.001	
>5cm	89 (21.50%)	0	72.9836	<0.001	
Total diameters of multiple tumors			50.6905	<0.001	
≤5cm	72 (45.00%)	186 (70.19%)	26.5356	<0.001	
>5cm and ≤10cm	66 (41.25%)	79 (29.81%)	5.8074	0.016	
>10cm	22 (13.75%)	0	38.4266	<0.001	
Child classification			78.5092	<0.001	
A	242 (42.16%)	191 (33.99%)	8.0447	0.005	
B	332 (57.84%)	300 (53.38%)	2.2874	0.13	
C	0	71 (12.63%)	77.3504	<0.001	
MELD score	12.11±3.08	13.20±5.24	-4.2847	<0.001	
CCI	2.42±1.10	2.67±1.26	-3.5646	<0.001	
Surgical methods					
Regular liver lobe resection	222 (38.68%)				
Irregular liver lobe resection	352 (61.32%)				
RFA approach					
Percutaneous		384 (68.33%)			
Laparotomy		178 (31.67%)			
Laparotomy RFA methods					
Simple laparotomy RFA		63 (35.39%)			
Partially liver resection combined with RFA		46 (25.84%)			
Pericardial devascularization combined with RFA		69 (38.76%)			
Abbreviations:PBC = Primary biliary cirrhosis; AFP = alpha-fetoprotein; MELD = Model for end-stage liver disease; CCI = Charlson Co-morbdity Index.					

Table 1: Demographic Characteristics

RF ablation procedure

Percutaneous RFA indications

In our institution, the indications for RFA treatment of solitary HCC includes: (a) Patients with Child-Pugh class A/B; tumor size ≤5 cm; no invasion into intrahepatic vessels and/or bile duct seen on abdominal CT or MRI; tumor located deep in the right lobe of the liver and adjacent to the main intrahepatic vessels;the left hepatic lobe had significant hyperplasia and tumor involvement with at least 3 normal liver segments that would have to be removed if surgical resection was to be performed. (b) Patients in Child-Pugh class C; tumor size ≤5 cm; no invasion into intrahepatic vessels and/or bile duct seen on abdominal CT or MRI; and liver function restored to Child-Pugh class B after 2 weeks of medical treatment.

RFA indications for multiple tumors were as follows: (a) Child-Pugh class A/B subjects; single tumor size ≤3 cm; numbers of cancer nodules ≤3; total diameter of all tumors ≤10 cm; tumors located deep in both the right and left liver lobes; no invasions into intrahepatic vessels and/or bile duct seen on abdominal CT or MRI, and at least 3 normal liver segments that would have to be removed during surgical resection. (b) Subjects in Child-Pugh class C; single tumor size <3 cm; number of cancer nodules ≤2; the total diameter of all tumors ≤5 cm; no invasion into intrahepatic vessels and/or bile duct seen on abdominal CT or MRI, and liver function restored to Child-Pugh class B after 2 weeks of medical treatment.

Combined therapy of partial liver resection and RFA indications for multiple tumors Child-Pugh class A/B subjects; single tumor size ≤3 cm, numbers of cancer nodules ≤3; total diameter of all tumors ≤10 cm; tumors distributed in both the right and left liver lobes; no invasion into intrahepatic vessels and/or bile duct seen on abdominal CT or MRI. The 1–2 cancer nodules located deep in the liver parenchyma were treated with RFA. Other tumors located on the surface of the liver were removed through surgical resection.

Combined therapy of devascularization and RFA indications for HCC associated with PHChild-Pugh class A/B subjects with history of bleeding from esophagogastricvarices caused by PH, single tumor size ≤3 cm; numbers of nodules ≤2, total diameter of all tumors ≤5 cm; no invasions into intrahepatic vessels and/or bile duct seen on abdomen CT or MRI, or tumors located deep in the liver parenchyma. Splenectomy and pericardial devascularization was performed. RFA therapy was performed to destroy the cancer nodules.

RFA technique

Ultrasound was performed prior to the procedure. For subjects whose Child-Pugh classes had improved from C to B after 2 weeks of conservative treatment, the RFA procedure was performed percutaneously under ultrasound guidance. For the following two groups of subjects, RFA was approached by laparotomy: (a) Subjects with tumors located adjacent to the middle hepatic vein and right hepatic vein with major part of the normal liver tissue that had to be removed during surgical resection; (b) subjects with obvious right liver lobe atrophy and significant left liver lobe hyperplasia with tumors located close to the left and middle hepatic veins and in whom the whole left lobe of the liver had to be removed during surgical resection. The RFA were approached through laparotomy because the percutaneous approach could cause thermal injuries to the diaphragm and the heart. During the laparotomy RFA, the liver was separated to expose the tumors completely. The diaphragm and the heart were protected appropriately, and RFA was performed under ultrasound guidance. The RFA device model used in this study was the US CTRF-220 cooled electrodes RF system. The ultrasound model used was L0GIQ.S6 (General Electric, Inc.). The RFA procedures were performed by one radiologist and one surgeon, who had 5 years of experience in interventionaltherapy at the start of the study. The methods were the same as those described in other research reports [14]. Ultrasounds were performed 5 minutes after the RFA procedures, and the images showed the tumors to be completely ablated. The ablated zones (hyperechoic zone on image) were 1–1.5 cm over the borders of the tumors, which indicated that the procedures had been successful.

Surgical resection

Surgical resection was carried out through a bilateral subcostal incision with the patient under general anesthesia. Intraoperative ultrasound was performed to evaluate the tumor burden, the liver remnant, and the possibility of a negative resection margin. Anatomic resection, in the form of segmentectomy or subsegmentectomy as described by Makuuchi et al. [15], was the preferred surgical method for liver resection. The Pringle maneuver was routinely used, with clamping and unclamping times of 10 and 5 minutes, respectively. This technique was used repeatedly throughout the entire procedure. Hemostasis of the surface of the raw liver was achieved with suturing.

Postoperatively, all resected specimens were evaluated under a conventional histopathologic examination. According to the guidelines of the International Union Against Cancer, complete resections, here designated R0, were defined by the absence of microscopic tumor invasion of the margins of the resected area (tumor-free margins 1 mm for all lesions detected) [16].

Efficacy and follow-up

Major complications were defined as complications that were life threatening, that led to substantial morbidity or disability, or that lengthened the hospital stay [17]. All other complications were considered minor. Pain was graded as absent or mild if the patient did not require any analgesics because moderate or severe if analgesics were necessary to relieve the pain [18]. Fever was defined as an axillary temperature of more than 38.5°C. All complications were observed clinicallywhen patients were admitted andassessed by telephone interview afterpatients were discharged.

The patients were followed up once a month, and the tests conducted included routine blood tests, liver function tests, assessments of AFP levels, and imaging. Liver damage was classified by Child-Pugh classification. Child-Pugh class A, B and C indicated that the liver function was mild damage, moderate damage and severe damage (liver failure), respectively.The abdominal CT or MRI was obtained one month after the procedure. If no tumor remnants were found, ultrasound was performed every month, and enhanced abdominal CT or MRI was obtained every three months. If no recurrences, metastasis, or new neoplasms were seen after six months, ultrasound was performed every three months from then on, and a CT or MRI was obtained every six months.

Local tumor recurrence was defined as the appearance of tumor growth around the original ablated area in the RFA group, and at the resected liver surface after resection in the SR group. Distant recurrence was defined as the appearance of new HCC in the untreated liver or extrahepatic regions [19].The following observation was recorded: general wellness, post-procedure complications, prognosis, tumor remnants, total survival rates, and tumor-free survival rates.

Statistical analysis

Statistical analyses were performedusing SPSS 11.0(SPSS Inc, Chicago, IL, U.S.). The two groups werecompared using the Student t testfor continuous data and the Chi-square or Fisher's exact test forcategorical data. Overallsurvival was evaluated from the day of surgery or RFA to the day of death or to the day of the last follow-up or to the most recentfollow-up visit. There were 192 patients lost to follow-up (85 of 574 patients in the SR group; and 107 of 562 patients in the RFA group). Tumor-free survival was computed from theday of surgery or RFA to the first follow-up visit at which evidence of a tumor was clear or themost recent follow-up visit. Death without recurrence endedthe observation. Survival rates were calculated using the life table method and differences between the groupswere assessed with the Wilcoxon's test. Results are given asmedians ± standard deviations. Allstatistical tests were two-sided, and differences were consideredsignificant at P<0.05.

Results

Demographic characteristics of the patients are listed in Table 1. Mean age and AFP level were not significantly different and hepatitis B virus (HBV) was the main cause of cirrhosis. There was significant difference in the MELD score (P<0.001) andCCI (P<0.001) between the two groups. Although the rate of patients with Child-Pugh class B was similar in the two groups (57.84% vs 53.38%, respectively, P=0.130), the rate of patients with Child-Pugh class A was higher in the SR group (42.16%) than in the RFA group (33.99%) (P=0.005)), and all the 71 patients with Child-Pugh class C were distributed in the RFA group.

There were no cases of perioperative deaths within 30 days of treatment in either group. Major complications occurred more in the SR group (71 of 574 patients) than in the RFA group (38 of 562 patients) (P = 0.001), and the rate of liver failure in major complications was higher in the SR group (18.31%) than in the RFA group (10.53%) (P= 0.048) (Table 2). There was no evidence of tumor-track seeding after RFA. Pain and fever were the most common minor complications after treatment. Post-treatment fevers of more than 38.5°C were observed in 242 patients in the SR group and 173 in the RFA group (P<0.001). After treatment, 267 patients in the SR group and 98 in the RFA group required the administration of analgesics (P<0.001) (Table 2).

Variable	SR group (n=574)	RFA group (n=562)	χ^2 value	P value
Mortality	0	0		
Major complication	71	38	10.2946	0.001
liver failure	13	4		0.048
Peritoneal bleeding	6	4		0.753
Gastrointestinal bleeding	5	5		1
Intestinal obstruction	2	0		0.5
Bile leakage	6	2		0.288
Abdominal infections	9	6		0.605
Lung infection	11	6		0.329
Urinary tract infection	3	3		1
Moderate/severe hydrothorax	8	3		0.225
Rupture of incision	2	0		0.5
Infection of incision	6	5		1
Minor complication				
Fever	242	173	15.8535	<0.001
Moderate/severe pain	267	98	110.105	<0.001

Table 2: Post-treatment complications

In the SR group, there were 72 subjects with mild liver damage, 489 with moderate damage, and 13 with severe damage. In the RFA group, there were 388 subjects with mild damage, 170 with moderate damage, and 4 with severe damage. The difference between these two groups (χ^2=40.8913, P<0.001) was significant.

The follow-up rate and length were 85.19% (489/574) and 4.8±1.0 years for the SR group and 80.96% (455/562) and 5.0±2.2 years for the RFA group. There was no significant difference in the follow-up rate (χ2=0.3342, P=0.0563) or length (t=-1.8186, P=0.0693) between the two groups. Among all follow-up cases, no tumor remnants were found in enhanced abdominal CT or MRI one month after the procedure in the SR group, but 41 nodules with remnants were found in 23 subjects in the RFA group. The median survival times were 56.08 months for the SR group, and 57.81 months for the RFA group. The 1-, 2-, 3-, 4-, and 5-year total survival rates in the SR group were 94%, 85%, 72%, 39%, and 31%, respectively; and the survival rates in the RFA group were 87%, 82%, 68%, 46%, and 43%, respectively. No significant difference in any survival rate was observed between the two groups (μ=3.393, P=0.065) (Figure 1). The tumor-free median survival times were 52.49 months for the SR group and 49.92 months for the RFA group. The 1-, 2-, 3-, 4-, and 5-year tumor-free survival rates in the SR group were 77%, 64%, 61%, 31%, and 28%, respectively; and the survival rates in the RFA group were 66%, 63%, 53%, 36%, and 23%, respectively. The difference between two groups was significant (μ=5.270, P=0.022) (Figure 2).

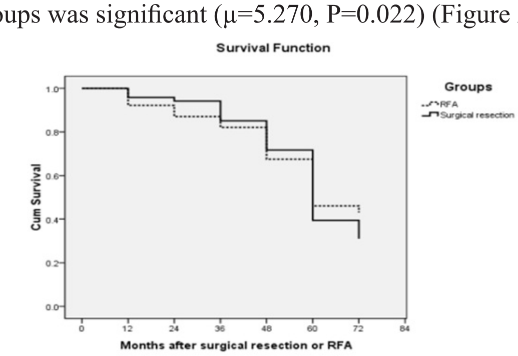

Figure 1 Post-procedure total survival rate

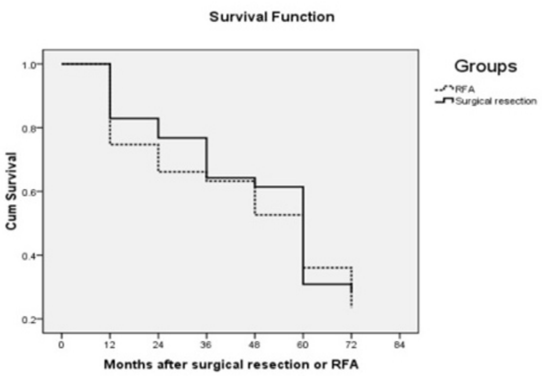

Figure 2 Post-procedure tumor free survival rate

Discussion

China has high hepatitis B virus (HBV) endemicity, with approximately 9.8% of the population chronically infected (i.e. hepatitis B surface antigen (HBsAg) positive for more than 6 months). Around 120 million people in China are carriers of HBV, amounting total most a third of all HBV-infected people worldwide[20]. HBV transmission is a leading cause of mortality and morbidity in China, with about 300,000 deaths annually attributable to HBV-related diseases, including 180,000 from HCC[20]. HBV can cause HCC in the absence of cirrhosis, although most cases of HBV-related HCC (70%–90%) occur in patients with cirrhosis[21].The patients' liver function may deteriorate after surgery, and sometimes may even result in liver failure [22-24]. For HCC patients associated with cirrhosis, it is critical preserve normal liver tissues and avoids liver failure after surgery. Although there are many reports evaluating of hepatic function and the amount of liver removal, there is still no ideal means to assure adequate liver function[25-26]. The issue of whether treating HCC through surgical resection of large segments of normal liver parenchyma especially when the tumors are adjacent to the intrahepatic main vessels, remains controversial. RFA therapy has the advantage of minor incisions, and it can completely ablate the tumor tissue. For this reason, it is the main treatment for HCC in addition to surgical resection [27]. However, performing systematic assessments of HCC patients and creating individualized treatment plans to improve the efficacy of HCC treatment is still a matter of major clinical concern.

We studied 562 HCC patients treated with RFA (808 cancer nodules were ablated). These were compared to 574 HCC patients treated with partial liver resection. All subjects in both groups were diagnosed with HCC associated with cirrhosis. All procedures were performed successfully, and no 30-day mortality occurred in either group. There was no significant difference in the total survival rate between the two groups in follow-up visits($P=0.065$). This indicates that the effects of RFA are equivalent to those of surgical resection when performed appropriately, with candidates carefully selected and regular follow-up visits.

In this study, there was no evidence of tumor-track seeding after RFA which was confirmed by regular surveillancewith enhanced abdominal CT or MRI. Before treatment, the MELD score and CCI were higher in the RFA group than in the SR group($P<0.001$), however, the major complications occurred significantly more often in the SR group (71 of 574 patients) than in the RFA group (38 of 562 patients) ($P = 0.001$). Pain and fever were the most common minor complications after treatment. Aftertreatment, fevers of more than 38.5°C were observed in 242 patients in the SR group and 173 in the RFA group ($P<0.001$). After treatment, 267 patients in the SR group and 98 in the RFA group required the administration of analgesics ($P<0.001$). Although the surgical resection patients had good hepatic functional reserve before treatment, the patients were prone to have moderate or severe liver damage in post-procedure time. In the SR group, there were 72 subjects with mild liver damage, 489 with moderate damage, and 13 with severe damage. In the RFA group, there were 388 subjects with mild damage, 170 with moderate damage, and 4 with severe damage. The difference between these two groups ($P<0.001$) was significant. These data confirm that RFA has the advantage of minor incisions, quick recovery, and good curative effects in the treatment of HCC.

Among the 562 HCC subjects treated with RFA, the nodule diameter of single tumors was ≤5 cm, total nodule diameter in cases of multiple tumors was ≤10 cm, and 59.6% (177/297) of the subjects with single tumors had nodule sizes of ≤3 cm, 70.2% (186/265) of the subjects with multiple tumors had nodule diameters of ≤5 cm. Among the 574 subjects treated with surgical resection, 77.5% (321/414) of the subjects with single tumors had nodule diameters of >3 cm, 27.7% (89/321) of the subjects with single tumors had nodule sizes of >5 cm, and 13.7% (22/160) of subjects with multiple tumors had nodule diameters of >10 cm. The tumor-free survival rate in the surgical group was higher than in the RF group ($P=0.022$).This indicates that surgical resection continues to be the standard of care for the treatment of HCC. This is because it has better curative effects and is associated with better long-term prognosis.

One of the contraindications of surgical resection is Child-Pugh class C status. For patients with HCC that meet the Milan criteria, liver transplant is the appropriate treatment [28-29]. However, the high cost of liver transplantation and the small number of liver donors makes liver transplantation difficult, especially in developing countries. In this study, 12.6% (71/562) of the subjects treated with RFA were Child-Pugh class C. However, two weeks of conservative treatment according to the Korean guideline for the treatment liver cirrhosis[30] improved their status to Child-Pugh class B. These subjects were treated with percutaneous RFA without post-procedure liver failure. This confirms the advantage of minimally invasive RFA over other treatments. Patients with terminal liver diseases associated with HCC can still receive RFA treatment after appropriate liver protective treatment, allowing them to live long enough to wait for a liver donor. This is consistent with other reports [31]. Among 71 subjects in Child-Pugh class C, the size of single tumors was ≤3 cm. For subjects with multiple tumors, the number of cancer nodules was ≤2, tumor size was <3 cm, and total tumor size was ≤5 cm. For subjects whose liver function changed from Child C to Child B, extra caution must be taken when planning treatment.

In 2011, "Expert consensus on local ablation therapy for hepatocellular carcinoma" was published by the Chinese Society of Liver Cancer, Chinese Society of Clinical Oncology, and Chinese Society of Hepatology. It discusses strategies of regulating local ablation therapy for HCC. The RFA indications of the 562 subjects were consistent with experts' views. This is one of the main reasons why the effects of RFA treatment observed in this study were equivalent to those of surgical resection. The treatment plans were created based on each subject's clinical characteristics. In the present study, percutaneous RFA was selected for subjects with puncture approaches observed on sonograms. Laparotomy RFA was selected for subjects with tumors located close to the diaphragm, which would have required resection of a large portion of the normal liver tissue. For some subjects, partial liver resection combined with laparotomy RFA was selected due to the tumor distribution. However, in enhanced abdominal CT and MRI images, which were made one month after the procedure, 41 cancer nodules with tumor remnants were found in 23 subjects with percutaneous RFA. The majority of these 23 subjects (16/23) received treatment before 2007, which was the early stage of the introduction of RFA. This may be especially true of tumors located close to the GI tract, gall bladder, diaphragm, and surface of the liver surface. It may be helpful to create individualized treatment plans to improve the effect of RFA on HCC.

The selection of treatment for HCC associated with PH is complicated [32]. For HCC patients with a history of PH and of bleeding from esophagogastricvarices, RFA combined with the surgical therapy may be appropriate if liver function is adequately compensated [33]. In China, the combined therapy of portal-azygous disconnection and irregular local partial resection is common. In this study, 69 subjects with PH received combined treatment involving splenectomy, pericardial devascularization, and RFA, and the effects were satisfactory. This combined therapy opens a new possibility of treating HCC patients with PH. It should be studied in more detail in the future.

The present study has limitations. First, it is a retrospective survey with all itsinherent limits and some selection bias, including the presence ofconfounding factors in the data, is unavoidable. Second, the patients were not uniformly treated. Surgical resectionpatients underwent anatomic or non-anatomic resection, and RFA patients were treatedwith percutaneous or laparotomy procedures. Third, only 64.8% of the RFA patients had any histological-diagnosis of HCC before treatment. All the patients without biopsy assessment inthis group had a non-invasive imaging pre-treatment diagnosis of HCC according to theguidelines in force at the time of enrollment. Fourth, the prolonged enrollment period required for the study could be an additional source of bias in the assessment of time-related variability in pre-treatment staging and post-treatment experiences. Fifth, this is asingle-center study. It is possible that these results may not apply to patientswith HCC in other countries becauseof differences in demographics and underlyingcauses of liver disease.Lastly, the high prevalence of censored data in thesurvival analysis may affect the reliability of the results of the study. However, this featureis an unavoidable consequence of the study population itself.

In conclusion, both surgical resection and RFA provide excellent short-term outcomes and facilitate long-term overall survival in patients with HCC complicated by cirrhosis. RFA appears to successfully ablate tumor and facilitate faster recovery less complications. Treatment efficacy is equivalent to that of surgical resection but the tumor-free survival rate is lower. This indicates that the choice between surgical resection and RFA should be tailored to the individual patient's characteristic. Percutaneous RFA is a reasonable option in patients with severe liver cirrhosis or centrally located tumors.It may be suitable for patients with either of the following: (a) tumors located adjacent to the middle hepatic vein and right hepatic vein and a major part of the normal liver tissue that must be removed during surgical resection; (b) obvious atrophy of the right liver lobe and significant left liver lobe hyperplasia with tumors located close to the left and middle hepatic veins and in whom the whole left liver lobe must be removed during surgical resection. Surgical resection is a feasible option in patients without advancedcirrhosis, with peripheral tumors, or with tumorslocated near the gallbladder, bowel loops, or the diaphragm. In these patients, RFA may be risky and less effective than surgical resection.

Acknowledgements

This work was supported by the Beijing Municipal Science and Technology Commission Capital Characteristic Clinical Application Research (No: Z121107001012169) and Capital Medical University, Beijing Ditan Hospital Research Fund Project (NO QN2011-04).

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