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W J C C World Journal of Clinical Cases

Contents

Semimonthly Volume 8 Number 19 October 6, 2020

OPINION REVIEW

4280 Role of monoclonal antibody drugs in the treatment of COVID-19 Ucciferri C, Vecchiet J, Falasca K

MINIREVIEWS

- 4286 Review of simulation model for education of point-of-care ultrasound using easy-to-make tools Shin KC, Ha YR, Lee SJ, Ahn JH
- 4303 Liver injury in COVID-19: A minireview Zhao JN. Fan Y. Wu SD

ORIGINAL ARTICLE

Case Control Study

4311 Transanal minimally invasive surgery vs endoscopic mucosal resection for rectal benign tumors and rectal carcinoids: A retrospective analysis

Shen JM, Zhao JY, Ye T, Gong LF, Wang HP, Chen WJ, Cai YK

4320 Impact of *mTOR* gene polymorphisms and gene-tea interaction on susceptibility to tuberculosis Wang M, Ma SJ, Wu XY, Zhang X, Abesig J, Xiao ZH, Huang X, Yan HP, Wang J, Chen MS, Tan HZ

Retrospective Cohort Study

4331 Establishment and validation of a nomogram to predict the risk of ovarian metastasis in gastric cancer: Based on a large cohort

Li SQ, Zhang KC, Li JY, Liang WQ, Gao YH, Qiao Z, Xi HQ, Chen L

Retrospective Study

4342 Predictive factors for early clinical response in community-onset Escherichia coli urinary tract infection and effects of initial antibiotic treatment on early clinical response

Kim YJ, Lee JM, Lee JH

- 4349 Managing acute appendicitis during the COVID-19 pandemic in Jiaxing, China Zhou Y, Cen LS
- 4360 Clinical application of combined detection of SARS-CoV-2-specific antibody and nucleic acid Meng QB, Peng JJ, Wei X, Yang JY, Li PC, Qu ZW, Xiong YF, Wu GJ, Hu ZM, Yu JC, Su W
- Prolonged prothrombin time at admission predicts poor clinical outcome in COVID-19 patients 4370 Wang L, He WB, Yu XM, Hu DL, Jiang H



World Journal of Clinical Cases		
Conter	nts Semimonthly Volume 8 Number 19 October 6, 2020	
4380	Percutaneous radiofrequency ablation is superior to hepatic resection in patients with small hepatocellular	
	carcinoma	
	Zhang YH, Su B, Sun P, Li RM, Peng XC, Cai J	
4388	Clinical study on the surgical treatment of atypical Lisfranc joint complex injury	
	Li X, Jia LS, Li A, Xie X, Cui J, Li GL	
4400	Application of medial column classification in treatment of intra-articular calcaneal fractures	
	Zheng G, Xia F, Yang S, Cui J	
4410	Clinical Irlais Study	
4410	Lakananurak N. Nalinthassanai N. Suansawang W. Panarat P.	
	META-ANALYSIS	
4416	Meta-analysis reveals an association between acute pancreatitis and the risk of pancreatic cancer	
	Liu J, Wang Y, Yu Y	
	SCIENTOMETRICS	
4431	Global analysis of daily new COVID-19 cases reveals many static-phase countries including the United	
4401	States potentially with unstoppable epidemic	
	Long C, Fu XM, Fu ZF	
	CASE REPORT	
4443	Left atrial appendage aneurysm: A case report	
	Belov DV, Moskalev VI, Garbuzenko DV, Arefyev NO	
4450	Twenty-year survival after iterative surgery for metastatic renal cell carcinoma: A case report and review	
	of literature	
	De Raffele E, Mirarchi M, Casadei R, Ricci C, Brunocilla E, Minni F	
4466	Primary rhabdomyosarcoma: An extremely rare and aggressive variant of male breast cancer	
	Satală CB, Jung I, Bara TJ, Simu P, Simu I, Vlad M, Szodorai R, Gurzu S	
4475	Bladder stones in a closed diverticulum caused by Schistosoma mansoni: A case report	
	Alkhamees MA	
4401		
4481	Cutaneous ciliated cyst on the anterior neck in young women: A case report	
4488	Extremely rare case of successful treatment of metastatic ovarian undifferentiated carcinoma with high- dose combination cytotoxic chemotherapy: A case report	

Kim HB, Lee HJ, Hong R, Park SG



. .	World Journal of Clinical Cases	
Conten	ts Semimonthly Volume 8 Number 19 October 6, 2020	
4494	Acute amnesia during pregnancy due to bilateral fornix infarction: A case report	
	Cho MJ, Shin DI, Han MK, Yum KS	
4499	Ascaris-mimicking common bile duct stone: A case report	
	Choi SY, Jo HE, Lee YN, Lee JE, Lee MH, Lim S, Yi BH	
4505	Eight-year follow-up of locally advanced lymphoepithelioma-like carcinoma at upper urinary tract: A case report	
	Yang CH, Weng WC, Lin YS, Huang LH, Lu CH, Hsu CY, Ou YC, Tung MC	
4512	Spontaneous resolution of idiopathic intestinal obstruction after pneumonia: A case report	
	Zhang BQ, Dai XY, Ye QY, Chang L, Wang ZW, Li XQ, Li YN	
4521	Successful pregnancy after protective hemodialysis for chronic kidney disease: A case report	
	Wang ML, He YD, Yang HX, Chen Q	
4527	Rapid remission of refractory synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome in response to the Janus kinase inhibitor tofacitinib: A case report	
	Li B, Li GW, Xue L, Chen YY	
4535	Percutaneous fixation of neonatal humeral physeal fracture: A case report and review of the literature	
	Tan W, Wang FH, Yao JH, Wu WP, Li YB, Ji YL, Qian YP	
4544	Severe fundus lesions induced by ocular jellyfish stings: A case report	
	Zheng XY, Cheng DJ, Lian LH, Zhang RT, Yu XY	
4550	Application of ozonated water for treatment of gastro-thoracic fistula after comprehensive esophageal squamous cell carcinoma therapy: A case report	
	Wu DD, Hao KN, Chen XJ, Li XM, He XF	
4558	Germinomas of the basal ganglia and thalamus: Four case reports	
	Huang ZC, Dong Q, Song EP, Chen ZJ, Zhang JH, Hou B, Lu ZQ, Qin F	
4565	Gastrointestinal bleeding caused by jejunal angiosarcoma: A case report	
	Hui YY, Zhu LP, Yang B, Zhang ZY, Zhang YJ, Chen X, Wang BM	
4572	High expression of squamous cell carcinoma antigen in poorly differentiated adenocarcinoma of the stomach: A case report	
	Wang L, Huang L, Xi L, Zhang SC, Zhang JX	
4579	Therapy-related acute promyelocytic leukemia with FMS-like tyrosine kinase 3-internal tandem duplication mutation in solitary bone plasmacytoma: A case report	
	Hong LL, Sheng XF, Zhuang HF	
4588	Metastasis of esophageal squamous cell carcinoma to the thyroid gland with widespread nodal involvement: A case report	
	Zhang X, Gu X, Li JG, Hu XJ	

Conton	World Journal of Clinical Cases
Conten	Semimonthly Volume 8 Number 19 October 6, 2020
4595	Severe hyperlipemia-induced pseudoerythrocytosis - Implication for misdiagnosis and blood transfusion: A case report and literature review
	Zhao XC, Ju B, Wei N, Ding J, Meng FJ, Zhao HG
4603	Novel brachytherapy drainage tube loaded with double 125I strands for hilar cholangiocarcinoma: A case report
	Lei QY, Jiao DC, Han XW
4609	Resorption of upwardly displaced lumbar disk herniation after nonsurgical treatment: A case report
	Wang Y, Liao SC, Dai GG, Jiang L
4615	Primary hepatic myelolipoma: A case report and review of the literature
	Li KY, Wei AL, Li A
4624	Endoscopic palliative resection of a giant 26-cm esophageal tumor: A case report
	Li Y, Guo LJ, Ma YC, Ye LS, Hu B
4633	Solitary hepatic lymphangioma mimicking liver malignancy: A case report and literature review
	Long X, Zhang L, Cheng Q, Chen Q, Chen XP
4644	Intraosseous venous malformation of the maxilla after enucleation of a hemophilic pseudotumor: A case report
	Cai X, Yu JJ, Tian H, Shan ZF, Liu XY, Jia J
4652	Intravesically instilled gemcitabine-induced lung injury in a patient with invasive urothelial carcinoma: A case report
	Zhou XM, Wu C, Gu X
4660	Bochdalek hernia masquerading as severe acute pancreatitis during the third trimester of pregnancy: A case report
	Zou YZ, Yang JP, Zhou XJ, Li K, Li XM, Song CH
4667	Localized primary gastric amyloidosis: Three case reports
	Liu XM, Di LJ, Zhu JX, Wu XL, Li HP, Wu HC, Tuo BG
4676	Displacement of peritoneal end of a shunt tube to pleural cavity: A case report
	Liu J, Guo M
4681	Parathyroid adenoma combined with a rib tumor as the primary disease: A case report
	Han L, Zhu XF

Contents

Semimonthly Volume 8 Number 19 October 6, 2020

ABOUT COVER

Peer-reviewer of World Journal of Clinical Cases, Prof. Adrián Ángel Inchauspe, obtained his MD in 1986 from La Plata National University (Argentina), where he remained as Professor of Surgery. Study abroad, at the Aachen and Tubingen Universities in Germany in 1991, led to his certification in laparoscopic surgery, and at the Louis Pasteur University in Strasbourg France, led to his being awarded the Argentine National Invention Award in 1998 for his graduate work in tele-surgery. He currently serves as teacher in the Argentine Acupuncture Society, as Invited Foreigner Professor at the China National Academy of Sciences and Hainan Medical University, and as editorial member and reviewer for many internationally renowned journals. (L-Editor: Filipodia)

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Retrospective Study

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ORIGINAL ARTICLE

Percutaneous radiofrequency ablation is superior to hepatic resection in patients with small hepatocellular carcinoma

Yan-Hua Zhang, Bo Su, Pei Sun, Ru-Meng Li, Xiao-Chun Peng, Jun Cai

ORCID number: Yan-Hua Zhang 0000-0003-3468-903X; Bo Su 0000-0002-7608-0487; Pei Sun 0000-0003-1130-2277; Ru-Meng Li 0000-0003-1461-8445; Xiao-Chun Peng 0000-0001-9443-0439; Jun Cai 0000-0002-9652-0910

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Yan-Hua Zhang, Jun Cai, Department of Oncology, First Affiliated Hospital, Yangtze University, Jingzhou 434023, Hubei Province, China

Bo Su, Pei Sun, Ru-Meng Li, Xiao-Chun Peng, Laboratory of Oncology, Center for Molecular Medicine, School of Basic Medicine, Yangtze University, Jingzhou 434023, Hubei Province, China

Corresponding author: Jun Cai, MD, PhD, Professor, Department of Oncology, First Affiliated Hospital, Yangtze University, No. 1 Nanhuan Road, Jingzhou 434023, Hubei Province, China. 2911152289@qq.com

Abstract

BACKGROUND

It is not known whether percutaneous radiofrequency ablation (PRFA) has the same treatment efficacy and fewer complications than laparoscopic resection in patients with small centrally located hepatocellular carcinoma (HCC).

AIM

To compare the effectiveness of PRFA with classical laparoscopic resection in patients with small HCC and document the safety parameters.

METHODS

In this retrospective study, 85 patients treated with hepatic resection (HR) and 90 PRFA-treated patients were enrolled in our hospital from July 2016 to July 2019. Treatment outcomes, including major complications and survival data, were evaluated.

RESULTS

The results showed that minor differences existed in the baseline characteristics between the patients in the two groups. PRFA significantly increased cumulative recurrence-free survival (hazard ratio 1.048, 95% CI: 0.265-3.268) and overall survival (hazard ratio 0.126, 95% CI: 0.025-0.973); PRFA had a lower rate of major complications than HR (7.78% vs 20.0%, P < 0.05), and hospital stay was shorter in the PRFA group than in the HR group $(7.8 \pm 0.2 \text{ d } vs 9.5 \pm 0.3 \text{ d}, P < 0.001)$.

CONCLUSION

Based on the data obtained, we conclude that PRFA was superior to HR and may reduce complications and hospital stay in patients with small HCC.



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Core Tip: In this retrospective study, the effectiveness of percutaneous radiofrequency ablation (PRFA) with classical laparoscopic resection in patients with small hepatocellular carcinoma (HCC) was compared and the safety parameters determined. PRFA treatment reduced the incidence of complications compared with resection and significantly improved overall survival as well as recurrence-free survival. Therefore, PRFA was superior to hepatic resection and may reduce complications and mortality in patients with small HCC.

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INTRODUCTION

Hepatocellular carcinoma (HCC) has a high mortality among all cancers worldwide^[1]. Most patients with HCC have decreased liver function and require treatment to completely excise the lesion and effectively mitigate further damage to the liver^[2]. Hepatic resection (HR) is recommended for patients with a single small HCC lesion up to 2 cm, which is a curative strategy and prevents recurrences. However, the operation takes a heavy toll on the patient's body. Therefore, clinicians have employed other methods including percutaneous radiofrequency ablation (PRFA), percutaneous ethanol injection, and laparoscopic radiofrequency ablation (LRFA) therapy^[3]. PRFA therapy is effective for controlling local tumours with improved survival and is the current standard for early-stage HCC requiring ablative treatments^[4-11]. Although studies have demonstrated the superiority of LRFA to PRFA for patient survival^[12], LRFA is more invasive than PRFA with higher risks of complications and requires general anaesthesia^[13]. When percutaneous ablation treatments cannot be used, HR is a suitable alternative for the treatment of small HCC^[14]. However, the most optimal treatment for patients with HCC has not been fully investigated. Thus, we aimed to compare the effectiveness and safety of PRFA with HR and investigate the recurrence, mortality, and survival rates in patients with HCC.

MATERIALS AND METHODS

Patients

We enrolled 175 patients with small HCC in our hospital from July 2016 to July 2019, of whom 85 received HR and 90 were treated with PRFA. This study was approved by the ethics committee of Yangtze University (Jingzhou, China) and all patients provided informed written consent to participate in this study.

Hepatic resection and percutaneous radiofrequency ablation treatment

For HR, patients were placed under general anaesthesia, a 1 cm sub-umbilical incision was made, and a trocar with a diameter of 1 cm was inserted to determine the location of the tumour. The hepatic ligament was then removed and labelled on the surface of the liver 2 cm adjacent to the tumour. Finally, we completely resected the entire hepatic segment or lobe^[15]. For PRFA we used computed tomography (CT) or magnetic resonance imaging (MRI) for ultrasonography guidance in real-time. We intercostally or subcostally inserted a 17-gauge cooled-tip electrode of 2-3 cm. The ablation procedures generally lasted 12 min with a 3 cm electrode and 6 min with a 2 cm electrode, and a power of 80 W-100 W was typically used. The lesions were assessed one and eight weeks after PRFA by CT or MRI. We defined complete ablation as



hypoattenuation of the target area and the surrounding liver parenchyma, which was confirmed by radiology^[12].

Follow-up

During the 2.0 \pm 0.5-year follow-up period, the patients were followed up by CT or MRI examinations every 3-4 mo in the first two years after PRFA treatment. We also measured liver function and α-fetoprotein levels. Previously published definitions and guidelines were used to define patient outcome and oncologic response^[16]. CT or MRI during the follow-up period showing any tumour growth along the ablated or resected locations were considered recurrences and were managed accordingly depending on liver function and tumour characteristics.

Statistical analysis

All data were analysed by SPSS 20.0. We compared the continuous data of the two groups using the Student's *t*-test and the categorical data were examined by the χ^2 -test. Univariate logistic regression and multivariate Cox proportional-hazards regression were used to analyse the variables that significantly affected the recurrence or survival rates. The recurrence-free and overall survival were examined by Kaplan-Meier plot. Statistical significance was set at P < 0.05.

RESULTS

Patient characteristics

Table 1 compares the baseline characteristics of the study participants in the HR and PRFA groups. We observed that a higher proportion of patients who received HR had liver cirrhosis and multiple tumours (C2) and exhibited higher TNM stages compared with patients who received PRFA. These data were consistent with the results of liver function tests such as decreased albumin levels. Furthermore, we also found that the PRFA group showed lower AFP levels, which is a tumour marker for HCC. Additionally, there were no differences in the distribution or location of HCC tumours between the two groups. Patients who received PRFA had a significantly lower occurrence of complications compared with the HR group, which was paired with reduced hospitalisation duration.

Hepatocellular carcinoma recurrence during follow-up

Our univariate and multivariate analyses revealed that levels of serum albumin and AFP, the number of tumours (especially C2 tumours), and hospital duration in the PRFA group significantly affected the recurrence-free survival (Table 2). Similarly, the PRFA procedure, serum albumin and AFP levels, and hospital duration predicted overall survival of patients with HCC (Table 3).

Survival analysis

PRFA significantly increased cumulative recurrence-free survival (hazard ratio 1.048, 95%CI: 0.265-3.268) and overall survival (hazard ratio 0.126, 95%CI: 0.025-0.973) compared with HR (Figure 1) and was a significant predictor of both outcomes (Figure 2).

DISCUSSION

In recent years, clinicians have aimed for effective, precise, and minimally invasive treatments for patients with HCC, and PRFA and laparoscopic surgery have gradually become the primary recommended treatments^[17]. Compared with traditional open cholecystectomy, laparoscopic surgery is advantageous due to less trauma and bleeding and shorter recovery times with comparable survival and recurrence rates^[18]. PRFA is a newly developed local treatment that relies on heat to induce necrosis of the tumour and surrounding tissues and has been demonstrated to achieve the same clinical effect as open surgery for patients with single small HCC up to 3 cm in size^[19,20]. PRFA can be easily performed and is repeatable with little damage to liver function^[21]. However, the best choice of therapy for patients with HCC requires further study.

In this study, we found that hospitalization duration was significantly shorter and complications were less frequent in the PRFA group than in the HR group, and this



Table 1 Baseline characteristics of the study participants, n (%)			
	HR (<i>n</i> = 85)	PRFA (<i>n</i> = 90)	P value
Gender (M/F)	47 (55.3)/38 (44.7)	52 (57.8)/38 (42.2)	0.740
Age (yr)	63.5 ± 7.6	62.8 ± 8.5	0.414
Cirrhosis aetiology			0.915
HCV	58 (68.2)	59 (65.6)	
HBV	12 (14.1)	13 (14.4)	
Other	15 (17.7)	18 (20)	
Platelet count (10 ³ /mm ³)	125 ± 58	118 ± 62	0.442
Total bilirubin (mg/dL)	1.05 ± 0.49	1.08 ± 0.51	0.692
PT (INR)	1.13 ± 0.06	1.14 ± 0.18	0.627
Albumin (g/dL)	3.87 ± 0.32	4.02 ± 0.40	0.007
AFP (ng/dL)	82.68 ± 7.85	80.24 ± 7.24	0.034
Tumour size (cm)	1.82 ± 0.24	1.76 ± 0.32	0.164
Number of tumours			0.012
1	63 (74.1)	82 (91.2)	
2	12 (14.1)	4 (4.4)	
≥3	10 (11.8)	4 (4.4)	
TNM stage			< 0.001
Ι	61 (71.8)	84 (93.3)	
П	24 (28.2)	6 (6.7)	
Subcapsular tumour	35 (41.2)	48 (53.3)	0.107
Complications	17 (20)	7 (7.78)	0.033
Postoperative haemorrhage	4 (4.71)	1 (1.11)	0.331
Bile leak	2 (2.35)	1 (1.11)	0.960
Subphrenic collection/abscess	3 (3.53)	1 (1.11)	0.573
Infected ascites	4 (4.71)	2 (2.22)	0.626
Liver failure	1 (1.18)	0 (0)	0.977
Pleural effusion	3 (3.53)	2 (2.22)	0.948
Hospital mortality	0	0	-
Days of hospital stay during initial therapy	9.5 ± 0.3	7.8 ± 0.2	< 0.001

HR: Hepatic resection; PRFA: Percutaneous radiofrequency ablation; HCV: Hepatitis C virus; HBV: Hepatitis B virus; PT: Prothrombin time; INR: International standardised ratio; AFP: Alpha fetoprotein.

> was consistent with the results of other studies^[22,23]. Also there were higher recurrence rates in patients treated by HR compared with PRFA. This could be due to the higher TNM stages of HCC tumours in patients treated with HR. Furthermore, these patients were more likely to have multiple tumours. PRFA did not significantly affect recurrence-free survival and was consistent with a previous study, although it did improve overall survival^[24]. However, PRFA may reduce HCC recurrence, which would lead to reduced patient mortality. Our data indicated that PRFA was a contributing and prognostic factor for improving overall survival, liver function, and tumour characteristics. Furthermore, local progression of HCC, intra-segmental recurrences, and recurrences less than 12 mo after treatment were more frequent after HR, which was not attributable to a selection bias. Studies have reported that HCC lesions less than 2 cm in diameter may harbour highly proliferative tumour cells, thus it is critical to locate micro invasions or microsatellites.

In conclusion, PRFA was superior to HR for the survival of small HCC patients,



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Table 2 Univariate logistic regression and multivariate Cox proportional-hazards regression for recurrence-free survival of patients with hepatocellular carcinoma who received hepatic resection or percutaneous radiofrequency ablation

Veriebles	Univariate logistic regression	Cox proportional-hazards regression	
variables	P value	Hazard ratio (95%CI)	P value
Albumin (g/dL)	0.018	0.325 (0.109-0.875)	0.020
AFP: normal vs abnormal	0.037	1.658 (1.135-3.258)	0.023
Number of tumours			
1		1.000	0.023
2		5.784 (1.387-20.268)	0.015
3		7.458 (0.896-87.257)	0.056
TNM stage	< 0.001		
Ι			
II			
Days of hospital stay during initial therapy	0.028	1.058 (1.005-1.224)	0.027
HR vs PRFA	0.043	1.045 (0.325-2.838)	0.039

AFP: Alpha fetoprotein; TNM: Tumor Node Metastasis; HR: hepatic resection; PRFA: Percutaneous radiofrequency ablation.

Table 3 Univariate logistic regression and multivariate Cox proportional-hazards regression for the overall survival of patients with hepatocellular carcinoma who received hepatic resection or percutaneous radiofrequency ablation

Variablaa	Univariate logistic regression	Cox proportional-hazards regression	
Valiables	<i>P</i> value	Hazard ratio (95%CI)	P value
Albumin (g/dL)	< 0.001	0.058 (0.008 - 0.425)	0.003
AFP: normal vs abnormal	0.0346	1.647 (1.057 - 3.269)	0.018
Days of hospital stay during initial therapy	0.013	1.325 (1.057 - 1.523)	0.006
HR vs PRFA	0.026	0.114 (0.015 - 0.846)	0.035

AFP: Alpha fetoprotein; HR: Hepatic resection; PRFA: Percutaneous radiofrequency ablation.

especially those with peripheral tumours. In addition, it safeguarded liver function and reduced the complication and recurrence rates compared with HR. Therefore, we recommend PFRA as the standard treatment for patients with HCC.

CONCLUSION

Based on the data obtained, we conclude that PRFA was superior to hepatic resection and may reduce complications and hospital stay in patients with small HCC. Therefore, increased clinical application of PFRA will prove PFRA as the standard treatment for patients with small HCC.



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Figure 1 Comparison of cumulative recurrence-free survival and overall survival of patients with hepatocellular carcinoma treated with hepatic resection or percutaneous radiofrequency ablation. A: Cumulative recurrence-free survival; B: overall survival of patients. PRFA: Percutaneous radiofrequency ablation; HR: Hepatic resection.



Figure 2 Kaplan-Meier curves of cumulative recurrence-free survival and overall survival of patients with hepatocellular carcinoma treated with hepatic resection or percutaneous radiofrequency ablation. A: Cumulative recurrence-free survival; B: Overall survival of patients. PRFA: Percutaneous radiofrequency ablation; HR: Hepatic resection.

ARTICLE HIGHLIGHTS

Research background

It is not known whether percutaneous radiofrequency ablation (PRFA) has the same treatment efficacy and fewer complications than laparoscopic resection in patients with small centrally located hepatocellular carcinoma (HCC).

Research motivation

This retrospective study aimed to compare the effectiveness of PRFA with classical laparoscopic resection in patients with small HCC and document the safety parameters, to provide an experimental basis for the clinical treatment of small HCC.

Research objectives

To determine whether PRFA has the same effect as surgical resection with fewer complications in patients with small HCC, in order to provide more specific options for HCC treatment.



Research methods

In this retrospective study, 85 patients treated with hepatic resection and 90 PRFAtreated patients were enrolled in our hospital from July 2016 to July 2019, Treatment outcomes, including major complications and survival data, were determined.

Research results

The results showed that minor differences existed in the baseline characteristics between the patients in the two groups. PRFA significantly increased cumulative recurrence-free survival (hazard ratio 1.048, 95%CI: 0.265-3.268) and overall survival (hazard ratio 0.126, 95% CI: 0.025–0.973); PRFA had a lower rate of major complications than HR (7.78 vs 20.0%, P < 0.05), and the hospital stay was also shorter in the PRFA group than in the HR group $(7.8 \pm 0.2 \text{ d } vs 9.5 \pm 0.3 \text{ d}, P < 0.001)$.

Research conclusions

Based on the data obtained, we conclude that PRFA was superior to hepatic resection and may reduce complications and hospital stay in patients with small HCC.

Research perspectives

The clinical application of PFRA should be increased to prove PFRA as the standard treatment for patients with small HCC.

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