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Original Article

CT-guided percutaneous chemical ablation combined with radiofrequency ablation for hepatocellular carcinomas in high-risk locations: lobaplatin vs. ethanol

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Abstract: To retrospectively compare the clinical efficacy and safety of CT-guided percutaneous injection of lobaplatin vs. ethanol for chemical ablation combined with radiofrequency ablation (RFA) in patients with hepatocellular carcinomas (HCCs) in high-risk locations. From January 2017 to June 2018, a total of 41 patients with HCCs in high-risk locations were enrolled and divided into two groups: percutaneous lobaplatin injection (PLI+RFA) group and percutaneous ethanol injection (PEI+RFA) group. The mixture of lobaplatin or ethanol was accurately injected into the high-risk part of the tumors, while RFA ablated the non-high-risk part. The efficacy and safety were compared between the two groups. 41 patients had 51 lesions in high-risk locations, including 24 cases with 30 lesions in PLI+RFA group and 17 cases with 21 lesions in PEI+RFA group. The complete ablation rate was 93.3% (28/30) in PLI+RFA group and 90.5% (19/21) in PEI+RFA group (P=1.000). The 2-year local tumor progression rate of PLI+RFA group and PEI+RFA group was 20.0% (6/30) and 19.0% (4/21), respectively (P=1.000). No significant differences were found in time to progression and overall survival between the two groups (P=0.501 and P=0.424, respectively). The incidence and severity of adverse events between the two groups were similar (P > 0.05). No severe complications were observed in both groups. Percutaneous lobaplatin injection combined with RFA in the treatment of HCC in high-risk locations may achieve the complete ablation rate similar to percutaneous ethanol injection combined with RFA, but further research is needed to confirm.

Keywords: Hepatocellular carcinoma, radiofrequency ablation, high-risk location, chemical ablation

Introduction

According to the global cancer statistics in 2018, liver cancer is one of the most common malignant tumors and the fourth leading cause of cancer-related death in the world [1]. Approximately 466000 new cases of liver cancer were annually diagnosed and 422000 annual deaths were reported in China, accounting for 55.4% and 53.9% of the world respectively, which seriously threatened the lives and health of the people [2]. Hepatocellular carcinoma (HCC) is the most common pathological type of primary liver cancer, accounting for 85-90% of all cases in China. Surgery is the first choice for treatment of HCC. However, radiofrequency ablation (RFA) has become an alternative first-line approach for curative treatment of HCC with BCLC at very early and early stage due to its advantages of minimal invasiveness, relatively low cost, exactly therapeutic efficacy and safety [3, 4]. But some tumors are located in challenging locations, such as subcapsular region or adjacent to the large blood vessels, gastrointestinal tract, gallbladder, diaphragm, heart, kidney, etc., which are considered as high-risk locations in clinical practice [5]. For tumors in high-risk locations, RFA may lead to injury to adjacent critical organs or incomplete ablation to avoid RFA-related complications [6-8]. HCC in high-risk location is common in clinical practice and was reported to be as high as 23.4-34.7% [8]. Many methods combined with RFA were applied to treat HCCs in high-risk locations. Among these methods, the combination of percutaneous ethanol injection (PEI) and

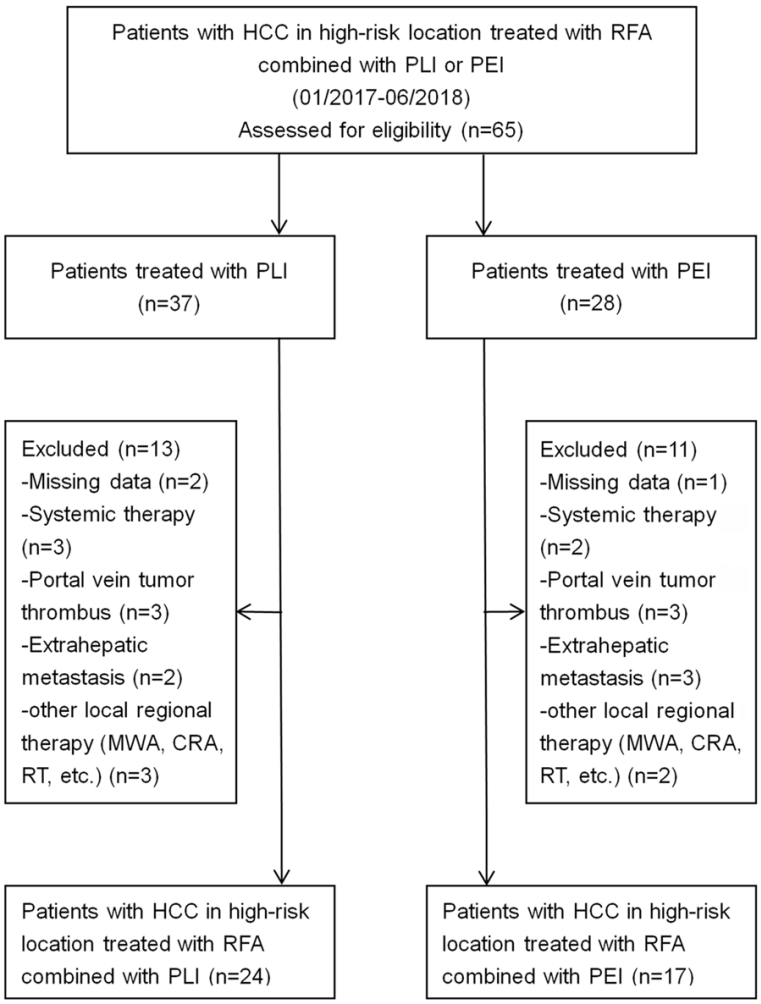

Figure 1. Flowchart shows patients selection. HCC, hepatocellular carcinoma; RFA, radiofrequency ablation; PLI, percutaneous lobaplatin injection; PEI, percutaneous ethanol injection; MWA, microwave ablation; CRA, cryoablation; RT, radiotherapy.

RFA was the widely used one [7-9]. PEI was actually performed to cover the whole tumor in previous literatures [7-9].

However, not all parts of the whole tumor in high-risk location are actually at high risk for RFA. The enrolled HCC tumors in high-risk locations were divided into two parts in our study as following: the high-risk part, presenting as the part that RFA is not safe to cover completely; the non-high-risk part, presenting as the part that RFA is safe to cover entirely. In our other study [10] for patients with HCCs in high-risk locations who were not suitable for or unwilling to undergo surgery, RFA was used to cover the non-high-risk part after ethanol was accurately injected into the high-risk part for chemical ablation. Compared with RFA alone, the complete ablation rate of the high-risk lesions was significantly improved without increasing complications. However, some patients may be allergic to ethanol so that there is a significant demand to develop a substitute for ethanol. It has previously been reported that chemotherapeutic drugs (epirubicin, cisplatin, mitomycin, lobaplatin, etc.) mixed with iodized oil were percutaneously injected directly into the tumor to treat primary or metastatic lesions (lymph node, adrenal gland, etc.) of HCC by chemical ablation [11-13]. Lobaplatin is not metabolized in the liver and could not aggravate liver damage [14]. More than 80% of patients with HCC were accompanied by liver cirrhosis in China [15]. Therefore, lobaplatin as a chemotherapy drug by locally direct injection for chemical ablation may be a better choice. In this study, lobaplatin or ethanol was accurately injected into the high-risk part of the tumor for chemical ablation, and then RFA was used to cover the non-high-risk part. The clinical efficacy and safety of lobaplatin versus ethanol chemical ablation combined with RFA were compared. Results of this study are reported as following.

Patients and methods

Study design

From January 2017 to June 2018, a total of 65 patients with HCCs in high-risk locations treated with RFA combined with percutaneous lobaplatin injection (PLI) or percutaneous ethanol injection (PEI) were retrospectively analyzed (**Figure 1**). HCC was diagnosed based on the noninvasive diagnostic criteria of the American Association for the Study of Liver Diseases (AASLD) or biopsy. The inclusion criteria included: (a) the definition of tumor in high-risk location was referred to the previous literature [5];

(b) patients ages ranged from 18 to 70 years; (c) the maximum size of tumor ≤ 5 cm; (d) number of nodules ≤ 3; (e) Child-Pugh A or B liver function status; (f) platelet count ≥ 50×10^9/l; (g) prothrombin time ratio over 50%; and (h) unwilling or unable to undergo radical surgery. The exclusion criteria included: (a) a history of allergy to iodine contrast agent, ethanol or lobaplatin; (b) a history of sorafenib or other systemic therapy; (c) received other local regional therapy (MWA, CRA, RT, etc.); and (d) portal vein tumor thrombus or extrahepatic metastases. This study was approved by the Medical Ethics Committee of Beijing Ditan Hospital (2018-025). According to the aforementioned inclusion and exclusion criteria, 41 patients with 51 HCC lesions in high-risk locations were enrolled in our study.

In this study, the part of the HCC lesion in high-risk location at a distance of less than 10 mm to the liver capsule, the first order branches of the portal vein, the main hepatic vein, or the inferior vena cava, or adjacent critical organs (including heart, diaphragm, kidney, gastrointestinal tract, gallbladder, etc.) was defined as "the high-risk part" while the other part of the lesion in high-risk location was defined as "the non-high-risk part".

All patients were informed of the advantages, disadvantages and complications of RFA combined with PLI or PEI. The choice of treatment regime was ultimately made by patients and their authorized relatives. All enrolled patients signed an informed consent form before treatment.

Transarterial chemoembolization (TACE)

TACE based on lipiodol was first conducted by two operators (JW and LC, with 15-20 years of relevant experience in interventional radiology) as previously described [16] in all patients except for two patients in each group who refused TACE. A visceral angiogram was performed to assess hepatic artery supply and then a microcatheter (2.7 Fr, Terumo Corporation, Japan) was coaxially sent through the 5-F catheter into the tumor feeding artery for superselective embolization with an emulsion of epirubicin (20-40 mg) (Pharmorubicin; Pfizer, Wuxi, China) and lipiodol (5-20 ml) (Lipiodol Ultra-Fluide; André Guerbet Laboratories, AulnaySous-Bois, France) until lipiodol retention was well displayed in the tumors. Absorbable embosphere microspheres (Biosphere Medical Inc., Rockland, MA) of 300-500 μm in diameter were used for embolization. The TACE procedure was performed in only one session.

Chemical ablation

CT-guided procedure with the combination of chemical ablation and RFA was performed by two physicians (WL and WS, with 12 and 8 years of ablation-related experience) 3-7 days after TACE. Single lesion was treated once while 2-3 lesions were treated twice within 7 days. 41 patients with 51 lesions in high-risk locations were divided into two groups as following: (1) PLI+RFA group (24 cases, 30 lesions). Based on the preoperative CT scan image, the optimal puncture plane and angle were set in real time. Once the 21G needle (Hakko, Japan) tip was guided into the high-risk part, the mixture of lobaplatin (10-20 mg) (Changan Hainan International Pharmaceutical Co., Ltd., Haikou, China) solution and iohexol (Jiangsu Hengrui Pharmaceutical Co., Ltd., Lianyungang, China) at the volumetric ratio of 19:1 was injected into the high-risk part of the lesion. The volume of the mixture was determined according to the volume of the high-risk part of the lesion. If necessary, multi-point injection or supplementary injection was performed to ensure the complete coverage of the high-risk part of the lesion. (2) PEI+RFA group (17 cases, 21 lesions). Except ethanol (99.5%, Sigma-Aldrich, St. Louis, MO, USA) and iohexol were mixed at the volumetric ratio of 19:1, the other procedure was the same as (1) above in this group. The iohexol of the mixture in both groups could be used as the tracer to display where lobaplatin or ethanol covered by CT scan.

Radiofrequency ablation

RFA was then applied to cover the non-high-risk part of the lesion with a bipolar OLYMPUS electrode (Celon AG Medical Instruments, Teltow, Germany) or multipolar Welfare electrode (WHK-3; Beijing Welfare Electronics Co., Ltd., Beijing, China) under CT (SIEMENS, SOMATOM Perspective 64, Germany) guidance. The procedure was performed under intravenous sedation and local anesthesia. The electrode output power and the ablation time were determined according to manual instructions. In non-high-risk part, 5-10 mm of the hepatic parenchyma

surrounding the lesion was covered by RFA as an ablative margin to ensure complete ablation.

Treatment response evaluation and follow-up

Contrast-enhanced CT or MRI scan was conducted one month after ablation as a reference standard for the treatment efficacy and every 3-6 months during follow-up. Response to treatment was classified as complete ablation or incomplete ablation according to the Society of Interventional Radiology Reporting Standards for image-guided ablation of tumor [17]. Adverse events and complications were analyzed according to NCI-CTCAE v4.03 guidelines [17]. The primary study endpoint was complete ablation rate at one month after the ablation procedure and the secondary study endpoints included 2-year local tumor progression rate, time to progression, overall survival and adverse reactions. The patient with incomplete ablation or local tumor progression could be treated again or transferred to surgery. But for patients with new multinodular lesions, portal vein or hepatic vein invasion, or extrahepatic metastasis, TACE, sorafenib, or conservative treatment was adopted. The last follow-up date was February 28, 2021.

Statistical analysis

Spss22.0 software was used for statistical analysis. Continuous measurement data were presented as mean ± standard deviation with normal distribution or as median (minimum-maximum) if non-normally distributed. Enumeration data were presented as percentages. The treatment efficacy rate and complication rate were compared between the PLI+RFA group and the PEI+RFA group with the χ^2 test and Fisher's exact test. Kaplan-Meier method was used to plot survival curve and survival analysis was performed by Log-rank test. $P < 0.05$ was considered to indicate statistical significance.

Results

Baseline characteristics

41 eligible patients were divided into PLI+RFA group (24 patients with 30 high-risk lesions) and PEI+RFA group (17 patients with 21 high-risk lesions). Among these patients, 34 were males and 7 were females. The median age was 56 years, ranged from 32 to 70. 35 patients had hepatitis B virus infection, 4 patients had hepatitis C virus infection and 2 patients had no hepatitis B or C virus infection. 33 cases had one high-risk lesion, 6 cases had two high-risk lesions and 2 cases had three high-risk lesions. Among 51 high-risk lesions, 18 tumors (35.3%) were abutting hepatic capsule, 11 tumors (21.6%) abutting heart and diaphragm, 10 tumors (19.6%) abutting major vessels, 7 tumors (13.7%) abutting gastrointestinal tract, and 5 tumors (9.8%) abutting gallbladder. No significant differences were observed between the two groups (all $P > 0.05$), as shown in **Table 1**.

Efficacy analysis

In PLI+RFA group, complete ablation was achieved in 28 of 30 high-risk lesions with one session of combination treatment (**Figure 2**). In PEI+RFA group, complete ablation was achieved in 19 of 21 high-risk lesions with one session of combination treatment (**Figure 3**). Two residual high-risk lesions for each group achieved complete ablation after additional session. The complete ablation rate in PLI+RFA group was similar to that in PEI+RFA group (93.3% and 90.5%, respectively; $\chi^2=0.140$, $P=1.000$). There was no significant difference in serum AFP level two months after first combination treatment between PLI+RFA group (10.9 ± 5.3 ng/ml) and PEI+RFA group (9.9 ± 4.2 ng/ml) ($t=0.627$, $P=0.535$); however, the serum level of AFP in both PLI+RFA and PEI+RFA groups was significantly lower than that before combination treatment ($t=3.524$, $P=0.002$; $t=5.198$, $P < 0.001$, respectively) (**Figure 4**).

The median follow-up period for all enrolled patients was 36 months (range, 16-49 months), with the median follow-up periods of 38 months (range, 16-49 months) in PLI+RFA group and 36 months (range, 18-48 months) in PEI+RFA group ($t=1.134$, $P=0.264$). The 2-year local tumor progression rate was 20.0% (6/30) in PLI+RFA group and 19.0% (4/21) in PEI+RFA group, with no significant difference ($\chi^2=0.007$, $P=1.000$). There was no statistic difference in time to progression between PLI+RFA group and PEI+RFA group ($P=0.501$; **Figure 5**). No significant difference was observed in overall survival between the two groups ($P=0.424$; **Figure 6**).

Safety evaluation

Grade-3 transaminase elevation and grade-3 abdominal pain were observed in few patients

Table 1. Baseline patient and disease characteristics [n (%)]

Parameter	PLI+RFA group (n=24)	PEI+RFA group (n=17)	χ^2/t	*P* value
Age# (mean ± SD), years	55.3 ± 9.8	54.1 ± 9.7	0.380	0.706
Sex			0.007	1.000
Male	20 (75)	14 (82.4)		
Female	4 (25)	3 (17.6)		
ECOG PS score			0.191	1.000
0	20 (75)	15 (88.2)		
1	4 (25)	2 (11.8)		
Child-Pugh class			0.017	0.896
A	16 (66.7)	11 (64.7)		
B	8 (33.3)	6 (35.3)		
Hepatitis virus status			0.562	0.755
HBV	20 (83.3)	15 (88.2)		
HCV	3 (12.5)	1 (5.9)		
non-HBV or HCV	1 (4.2)	1 (5.9)		
BCLC stage			0.133	1.000
A	22 (91.7)	15 (88.2)		
B	2 (8.3)	2 (11.8)		
Number of liver tumors			0.236	0.889
1	19 (79.2)	14 (82.4)		
2	4 (16.7)	2 (11.8)		
3	1 (4.2)	1 (5.9)		
High-risk location			0.139	0.998
Abutting gastrointestinal tract	4 (13.3)	3 (14.3)		
Abutting heart and diaphragm	6 (20.0)	5 (23.8)		
Abutting major vessels	6 (20.0)	4 (19.0)		
Abutting gallbladder	3 (10.0)	2 (9.5)		
Abutting hepatic capsule	11 (36.7)	7 (33.3)		
Tumor growth pattern			0.706	0.401
With capsule	12 (40.0)	6 (28.6)		
Infiltrative	18 (60.0)	15 (71.4)		
Largest diameter#, cm	3.0 ± 0.9	2.9 ± 1.0	0.490	0.627
AFP (ng/ml)#	404.1 ± 549.8	266.0 ± 203.6	0.986	0.330
≥ 200 ng/ml	14 (58.3)	10 (58.8)	0.001	0.975
TACE treatment			0.133	1.000
yes	22 (91.7)	15 (88.2)		
no	2 (8.3)	2 (11.8)		

Except where indicated, data are numbers of patients, with percentages in parentheses. #t-test, data are means ± standard deviations; ECOG PS, Eastern Cooperative Oncology Group performance status; HBV, hepatitis B virus; HCV, hepatitis C virus; AFP, a-fetoprotein; RFA, radiofrequency ablation; TACE, transarterial chemoembolization.

in both PLI+RFA group and PEI+RFA group while the other common adverse events were grade 2. No grade 4/5 adverse events were observed in both groups. All the adverse events were transient and were effectively relieved within 1-2 weeks by symptomatic treatment. The incidence and severity of adverse events in both groups were similar, and the differences were not statistically significant (all P > 0.05; **Table 2**). No severe complications were found in both groups.

Discussion

According to Chinese guidelines for the diagnosis and treatment of primary hepatic carcinoma

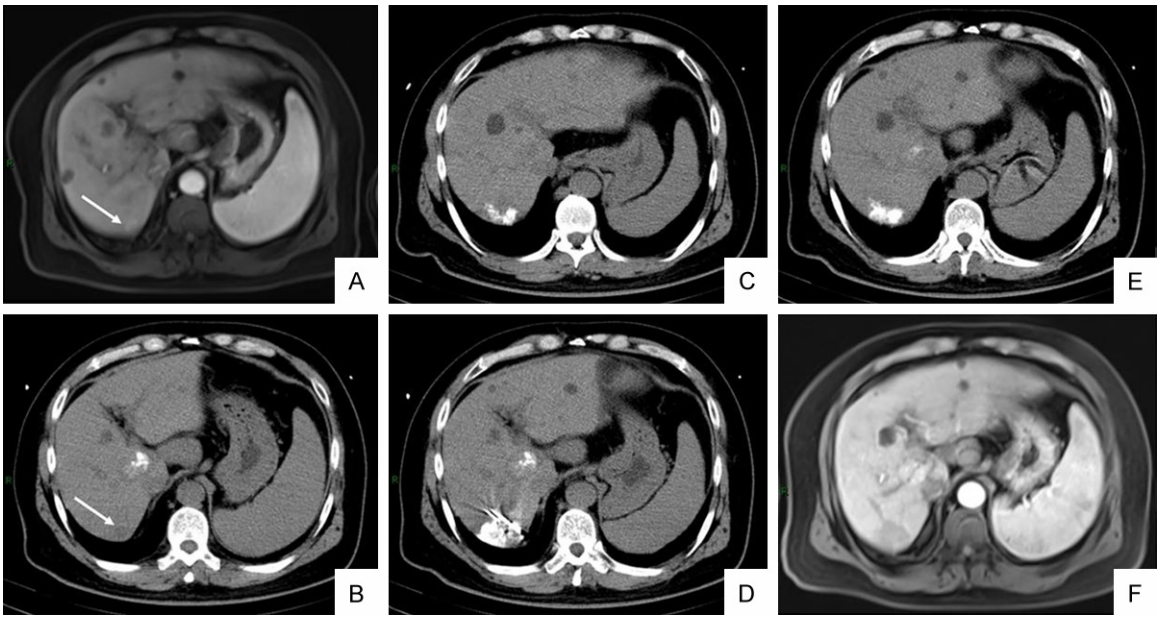

Figure 2. A 53-year-old male patient with HCC who underwent percutaneous lobaplatin injection (PLI) and RFA. (A, B) The lesion in S7 segment (white arrow) adjacent to diaphragm (A, MRI arterial phase; B, CT plain scan). (C) The high-risk part of S7 had been injected with lobaplatin. (D) The RFA needle was guided into the non-high-risk part of the tumor. (E) After treatment, CT scan was performed. (F) One month after operation, the tumor was completely ablated.

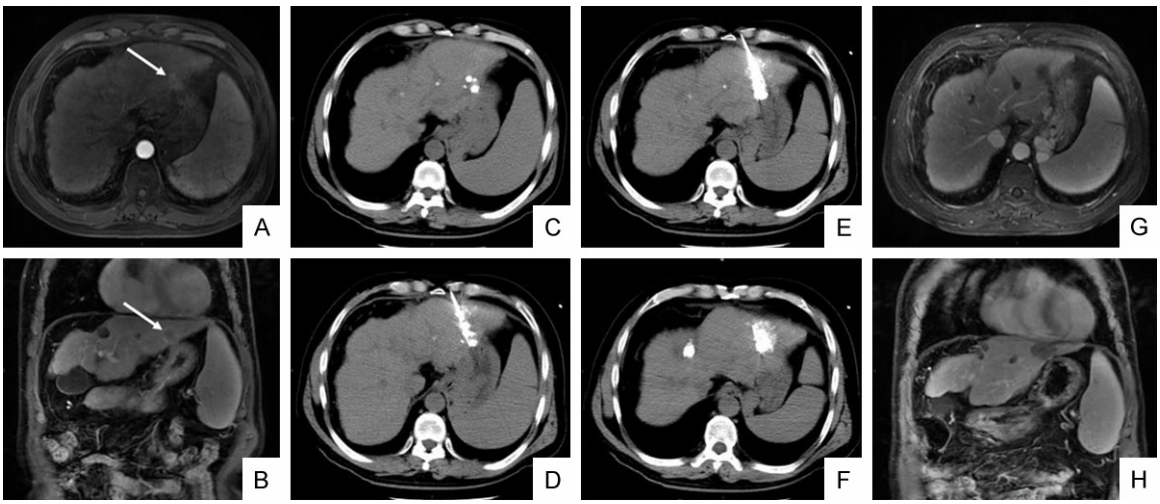

Figure 3. A 58-year-old male patient with HCC who underwent percutaneous ethanol injection (PEI) and RFA. MRI showed that the lesion (white arrow) in S2 segment was adjacent to the gastric wall in the transverse (A) and coronal (B) view. (C) After TACE, lipiodol retention was well displayed on the tumor site, but not dense enough. (D) The needle was guided into the high-risk part of the tumor. (E) The mixture of ethanol has been accurately injected. (F) The RFA needle was guided into the non-high-risk part of the tumor. One month after the operation, the tumor was completely ablated in the transverse (G) and coronal (H) view.

(2019 edition), RFA combined with or without TACE has become a radical therapy for HCC with stage IA, IB and IIA [18]. RFA usually needs 0.5-1.0 cm of ablative margin to achieve complete ablation of the index tumor. However, for liver tumors in high-risk locations, RFA would lead to injury to adjacent critical organs to achieve complete ablation or incomplete ablation for safety. These injury included puncture injury and thermal injury, and some may lead

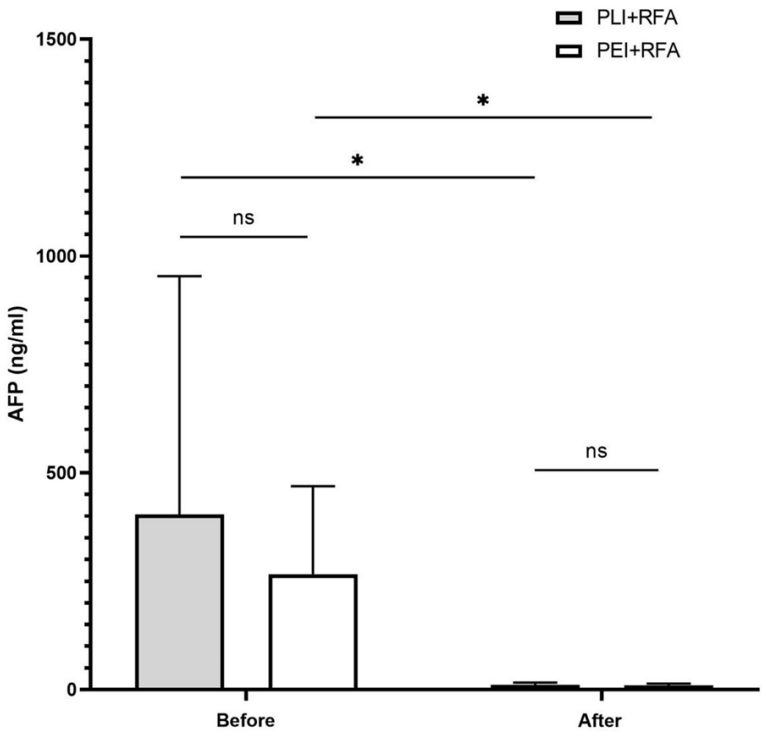

Figure 4. Changes of serum AFP level in both PLI+RFA and PEI+RFA groups after combination treatment. Note: ns, no significance; *, P < 0.05.

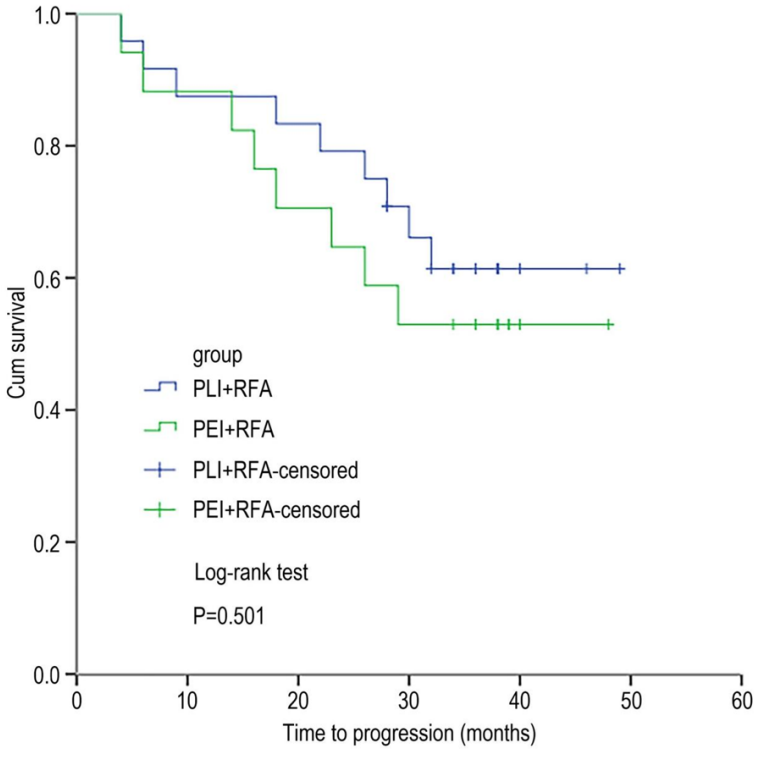

Figure 5. Cumulative time to progression curves in patients with HCCs treated with PLI+RFA or PEI+RFA.

to severe complications, such as hemoperitoneum, gastrointestinal perforation, liver abscess, pericardial tamponade, diaphragmatic perforation and even life-threatening conditions [5, 19-21]. In addition to the injury to blood vessels by the needle puncture, there is also a "heat sink" effect due to blood flow, which may lead to incomplete ablation of the lesions adjacent to blood vessels because of reduced temperature. Therefore, RFA for tumors in high-risk locations was challenging with high incidence of severe complications associated with adjacent organs or relatively low complete ablation rate [6-8]. The proportion of HCCs in high-risk locations reported in the literature was as high as 23.4-34.7% [8]. It is necessary to improve the complete ablation of HCCs in high-risk locations safely and efficiently. Some methods have been used in combination with RFA to improve the complete ablation rate of HCCs in high-risk locations with good safety. Effective methods reported previously included: TACE, ethanol injection, artificial ascites or pleural effusion, low-power RFA, balloon catheter intervention, fusion image-guided technology, laparoscopic or open approaches, etc. [8, 9, 22-28].

In fact, not all parts of the high-risk tumors are at high risk for RFA. Our previous study [10] suggested that for patients with HCCs in high-risk locations who were not suitable for or unwilling to undergo surgery, compared with RFA alone, the combination of percutaneous injection of ethanol into high-risk part

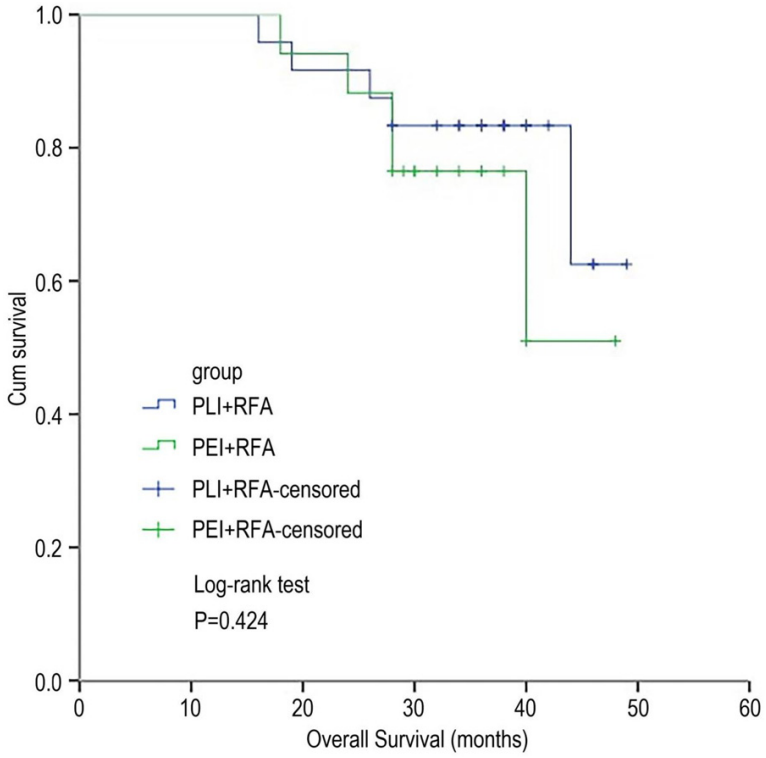

Figure 6. Cumulative overall survival curves in patients with HCCs treated with PLI+RFA or PEI+RFA.

(indicating that the part could not be safely covered by RFA) for chemical ablation and RFA for non-high-risk part (indicating that the part is safe for RFA and could be completely covered by RFA) could significantly improve the complete ablation rate of lesions in high-risk locations (93.2% vs. 73.9% respectively, P=0.014) without increasing major complications (0% vs. 6.7%, P=0.492). However, taking the fact into consideration that some patients are allergic to ethanol, it is necessary to develop a substitute for ethanol. Some reports showed that chemotherapy drugs (epirubicin, cisplatin, mitomycin, lobaplatin, etc.) mixed with iodized oil and directly injected into primary or metastatic lesions (lymph node, adrenal gland, etc.) of HCC for chemical ablation had good results [11-13]. In the literatures, ethanol (18 ml), lauromacrogol (2 ml), iodized oil (2 ml), lobaplatin (10 mg) and epirubicin (10 mg) were mixed into suspension at the volumetric ratio of 9:1:1:3:3. Over 80% patients with HCC were accompanied by cirrhosis in China [15]. Lobaplatin as a chemotherapy drug for local chemical ablation is a better choice because it is not metabolized in the liver and it would not aggravate liver damage [14]. In the present study, lobaplatin or ethanol was injected into the high-risk part of the lesion for chemical ablation, and then RFA covered the non-high-risk part. The clinical efficacy and safety of lobaplatin chemical ablation versus ethanol chemical ablation were compared.

In this study, iohexol was also used as a tracer for chemical ablation, which could display in real time whether the lobaplatin or ethanol mixture entirely covered the high-risk part of the lesion through CT scan. If not, the lobaplatin or ethanol mixture could be additionally injected so as to achieve complete ablation of the high-risk part. RFA was sequentially applied to achieve complete ablation of the non-high-risk part. Our study showed that the complete ablation rate with one session of combination treatment was 93.3% in PLI+RFA group and 90.5% in PEI+RFA group with no significant difference. The complete ablation rates of both groups were significantly higher than 70.6-73.9% of RFA group reported in the literature [7]. The 2-year local tumor progression rate in PLI+RFA group was similar to that in PEI+RFA group (20.0% and 19.0%, respectively). No statistic differences in time to progression and overall survival were observed between the two groups. In our study, the combination of lobaplatin or ethanol injection into the high-risk part of the lesions for chemical ablation and RFA for the non-high-risk part obtained the similar results in consistence with our previous research of iohexol-ethanol injection combined with RFA for HCCs in high-risk locations [7]. In contrast to the previous studies, less volume of the mixture was required for chemical ablation of the high-risk part of the index tumors.

In terms of safety, the incidence and severity of adverse events were similar between PLI+RFA group and PEI+RFA group. Except for a few patients with grade-3 transaminase elevation and grade-3 abdominal pain, adverse events of grade 1-2 were more common in both groups, which was consistent with the previous re-

Table 2. Comparison of common adverse reactions between PLI+RFA group and PEI+RFA group [n (%)]

Adverse Effect	PLI+RFA group (n=24)		PEI+RFA group (n=17)					
	Any grade (%)	Grade 3 (%)	Any grade (%)	Grade 3 (%)	Any grade (%)		Grade 3 (%)	
					χ^2	P	χ^2	P
Abdominal pain	18 (75)	2 (8.3)	11 (64.7)	1 (5.9)	0.509	0.507	0.088	1.000
Fatigue	18 (75)	0	14 (82.4)	0	0.314	0.711		
Nausea	17 (70.8)	0	11 (64.7)	0	0.173	0.678		
Vomiting	12 (50)	0	9 (52.9)	0	0.035	0.853		
Fever	21 (87.5)	0	15 (88.2)	0	0.005	1.000		
ALT elevation	22 (91.7)	6 (25)	14 (82.4)	3 (17.7)	0.806	0.633	0.314	0.711
AST elevation	20 (83.3)	4 (16.7)	12 (70.6)	2 (11.8)	0.944	0.450	0.191	1.000
Bilirubin elevation	10 (41.7)	0	7 (41.2)	0	0.001	0.975		

Note: ALT: alanine aminotransferase; AST: aspartate aminotransferase.

search of our department [7]. In this study, there were no major complications such as gastrointestinal perforation, gallbladder perforation, diaphragmatic perforation, pericardial tamponade, and hemoperitoneum in both groups, which could be associated with the small sample size. Another reason for good safety could be explained by the fact that RFA aimed not at the high-risk part of the lesion but at the non-high-risk part so that RFA could keep a safe distance from the adjacent organs which avoided damage of RFA puncture or thermal ablation. For the lesions adjacent to abdominal organs or diaphragm, our study did not adopt the isolation regime of artificial ascites or pleural effusion reported in the literature [25], but also achieved the similar therapeutic effect.

However, our study had some limitations. First, this study was a retrospective and small sample study conducted at a single institute, which could be affected by selection bias. All that our study obtained were only preliminary results. There was no direct head-to-head comparison to RFA alone for HCCs in high-risk locations. Therefore, prospective, large sample, multicenter and randomized controlled trials are required to confirm the results. Second, a few cases had pathological diagnosis, and most cases were diagnosed based on the noninvasive diagnostic criteria of the American Association for the Study of Liver Diseases (AASLD) because needle biopsy was not safe for the lesions in high-risk locations [29].

In conclusion, percutaneous lobaplatin injection into the high-risk parts of HCCs in high-risk locations for chemical ablation combined with RFA for non-high-risk parts could also obtain the complete ablation rate similar to percutaneous ethanol injection combined with RFA, which may be a safe and feasible therapeutic choice, especially for patients who are allergic to ethanol. Compared with RFA alone, another prospective large sample randomized controlled trial is ongoing to clarify the role of PLI combined with RFA for HCCs in high-risk locations (Project No. Z181100001718131 funded by the Beijing Municipal Science and Technology Commission).

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Disclosure of conflict of interest

None.

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