RESEARCH



The effect of continuous infusion chemotherapy through femoral artery catheterization on GP73, AFP-L3, and safety efficacy in liver cancer patients

Qiong Yan¹ · Xinguo Sun¹ · Yubo Wang² · Shijiao Duan¹ · Bo Wang³

Received: 6 December 2024 / Accepted: 6 January 2025 © The Author(s) 2025

Abstract

This study examines the impact of continuous infusion chemotherapy via femoral artery catheterization on Golgi protein 73 (GP73) and alpha fetoprotein heterogeneity (AFP-L3) in liver cancer patients. A retrospective analysis was conducted on 108 liver cancer patients treated from January 2020 to December 2022, divided into two groups: transarterial chemoembolization (TACE) and continuous infusion regional arterial chemotherapy via femoral artery catheterization (CIFAC), with 54 patients in each group. Serum tumor markers, liver function, adverse reactions, quality of life, and 1-year survival rate were analyzed and compared between the two groups of patients. Prior to treatment, no significant differences were observed in tumor markers, liver function, and quality of life between groups (P > 0.05). After 60 and 90 days, the CIFAC group exhibited significantly lower levels of GP73, AFP, and AFP-L3 compared to TACE (P < 0.05). Additionally, CIFAC patients had lower levels of alanine aminotransferase (ALT), aspartate transaminase (AST), indocyanine green (ICG15) (P < 0.05), reduced adverse reactions (nausea, vomiting, etc.), and higher Karnofsky scores (P < 0.05). The one-year survival rate of the CIFAC group was significantly higher than that of the TACE group (P < 0.05). Continuous infusion chemotherapy through femoral artery catheterization can help reduce serum tumor marker levels, improve liver function, and reduce adverse reactions in liver cancer patients.

Keywords Liver cancer \cdot Continuous infusion chemotherapy via femoral artery catheterization \cdot Serum tumor markers \cdot Liver function \cdot Adverse reactions

Introduction

Malignant tumors have always been a severe threat to the fitness of the Chinese people, among which primary liver cancer (PLC) ranks among the top. PLC mainly includes three types: hepatocellular carcinoma (HCC) [1], intrahepatic cholangiocarcinoma (ICC) [2], and HCC–ICC hybrid type [3]. Among them, HCC accounts for up to

main ways to treat PLC: curative treatment and palliative treatment. Radical treatment mainly includes surgical resection of tumors, liver transplantation, and radiofrequency ablation methods [5]. For patients who cannot receive curative treatment, palliative treatment becomes another option [6]. Among many palliative treatment methods, the treatment application of transarterial chemoembolization (TACE) [7] and the continuous infusion regional arterial chemotherapy via femoral artery catheterization (CIFAC) [8] is the most extensive. Early symptoms are not obvious, causing many patients to miss the opportunity for surgery when they experience obvious discomfort and seek medical attention, thus losing the opportunity to receive curative

85–90%. China accounts for 45.3% of the global total PLC cases and 47.1% of liver cancer deaths [4]. There are two

TACE is a commonly used local treatment method for liver cancer. This method mainly involves inserting

improving the prognosis of PLC patients [9].

treatment. This has also become the biggest challenge in

Published online: 10 May 2025



[☑] Bo Wang 17707340609@163.com

Interventional Catheterization Room, Affiliated Nanhua Hospital, University of South China, Hengyang 421002, China

Production Department, Guhan Traditional Chinese Medicine Co., Ltd, Hengyang 421000, China

³ Physical examination center, Affiliated Nanhua Hospital, University of South China, Hengyang 421002, China

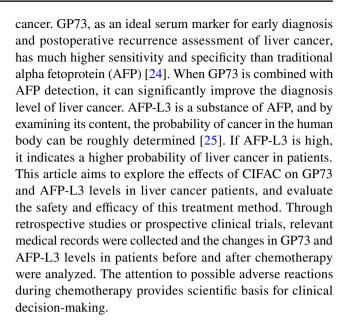
(2025) 25:148

a catheter into the tumor blood supply artery and then injecting embolic and chemotherapy drugs to achieve the goal of blocking the tumor blood supply and chemotherapy [10]. TACE uses drug-eluting microspheres loaded with chemotherapy drugs, which can slowly release chemotherapy drugs in tumor blood vessels, thereby achieving the effect of continuous chemotherapy [11].

CIFAC is a regional chemotherapy method that directly delivers chemotherapy drugs to the blood vessels of liver tumors, thereby increasing drug concentration in tumor tissue and reducing systemic side effects [12]. The main principle of CIFAC is that the normal liver receives dual blood supply from the hepatic artery [13] and portal vein [14], with hepatic artery supply accounting for 25% and portal vein supply accounting for 75%. In contrast, 95–99% of liver cancer's blood supply comes from the hepatic artery [15]. Meanwhile, by inserting a catheter into the hepatic artery, high concentrations of chemotherapy drugs can be directly delivered to the liver tumor tissue, which can increase the local drug concentration in the tumor tissue and reduce damage to normal liver tissue and other parts of the body [16]. The indications for CIFAC mainly include liver cancer patients with portal vein thrombosis, especially those with hepatic artery portal vein fistula or those who have received traditional interventional treatment but have poor efficacy [17]. In addition, CIFAC is also an effective treatment method for patients with liver metastasis from colorectal cancer [18]. For metastatic lesions of colorectal cancer that cannot be resected, using CIFAC can increase the local drug concentration of the lesion to tens of times that of peripheral venous chemotherapy, with advantages such as high local tumor control rate and minimal systemic side effects [19].

TACE is the best selection for treating advanced hepatocellular carcinoma. However, when the main portal vein or its primary branch is affected by cancer thrombi, TACE application is limited, which may lead to insufficient liver perfusion, causing serious problems such as acute liver failure and hepatic encephalopathy [20]. CIFAC is another type of interventional surgery that involves injecting anticancer drugs directly into the hepatic artery, increasing the concentration of drugs in the liver, enhancing treatment efficacy, and reducing systemic toxicity [21]. CIFAC is widely used in Japan, with commonly used drugs including epirubicin and cisplatin [22]. The 2013 EACH study confirmed that systematic chemotherapy based on oxaliplatin can bring survival benefits to liver cancer patients. Therefore, the application of CIFAC in treating advanced liver cancer with vascular invasion is gradually expanding [23].

Golgi apparatus transmembrane glycoprotein 73 (GP73) and alpha fetoprotein L3 (AFP-L3) are both serum markers correlated with the diagnosis and assessment of liver



Materials and methods

General information

Retrospective analysis was used to collect clinical basic data of 108 liver cancer patients admitted between January 2020 and December 2022 as the subjects of this study. In accordance with the differences in treatment, patients were segmented into TACE and CIFAC groups with 54 cases in each group. The patient or family member signed an informed consent form. The age range of TACE group is 38–74 years old, with an average of (51.44 ± 6.45) years old. There are 30 males and 24 females. Child-Pugh grading: 29 cases were classified as Grade A, 25 cases as Grade B, Barcelona staging (BCLC) 39 cases in stage B, and 15 cases in stage C with a disease course ranging from June to October, and an average disease course of (6.54 ± 1.41) months. Body mass index (BMI): $21.73 \pm 1.6 \text{ kg/m}^2$. The age range of the CIFAC group is from 40 to 75 years old, with an average of (53.46 ± 5.94) years old. There are 32 males and 22 females. Child-Pugh grading: Grade A with 31 cases, Grade B with 23 cases, Barcelona staging (BCLC) 37 cases in stage B, and 17 cases in stage C with a disease course ranging from May to November, and an average disease course of (6.76 ± 1.54) months. BMI: $21.85 \pm 1.40 \text{ kg/m}^2$. The general details of patients can be compared when P > 0.05. Inclusion criteria: ① The diagnosis of hepatocellular carcinoma must comply with pathological criteria or follow the relevant diagnostic criteria in the "PLC Diagnosis and Treatment Guidelines" [26] issued by the National Health Commission; 2 late-stage liver cancer patients who cannot be surgically removed and those who have not received other treatment methods at the initial



diagnosis; 3 physical condition must meet the scoring criteria of the Eastern Oncology Collaborative Group (ECOG) in the USA, ranging from 0 to 1; @ individuals without a history of autoimmune diseases; 3 those who are willing to adopt this treatment plan are required; and © patient's subjective consciousness voluntary cooperation indicators. Exclusion criteria: ① patients who are not suitable for femoral artery catheterization, such as those with femoral artery stenosis, occlusion, thrombosis, and other lesions; 2 individuals with severe organ dysfunction such as heart, lungs, liver, and kidneys who are unable to tolerate chemotherapy drugs; 3 individuals with inflammatory reactions such as infection and fever; @ individuals with poor physical conditions such as cachexia and malnutrition; (3) individuals with mental illness, cognitive impairment, etc. who are unable to cooperate with treatment; and @ pregnant women, lactating women and other special populations should be excluded.

Methods

Both groups of patients were given PD-1/PD-L1 inhibitors, such as a combination therapy of atezolizumab (Tecentriq) and bevacizumab (Avastin).

TACE group

Provide TACE treatment. After receiving general anesthesia or local anesthesia, the doctor inserts a catheter, which is usually inserted through the thigh artery or arm artery and guided into the hepatic artery through a vascular pathway. Inject contrast agent through a catheter and observe the condition of blood vessels and tumors through X-ray or other imaging techniques. Angiography can clearly display the location, size, and supply artery of liver cancer. After determining the location of liver cancer, the doctor directly injects chemotherapy drugs into the blood vessels of liver cancer patients through a catheter. Doctors will inject embolic agents to block the blood supply arteries of liver cancer, thereby blocking the tumor's blood supply, increasing the concentration of chemotherapy drugs at the liver cancer site, and reducing drug loss to normal liver tissue. Hepatocellular carcinoma treated with arterial chemotherapy and embolization every 4-6 weeks, lasting 2–5 times.

CIFAC group

The method of implementing CIFAC is to perform femoral artery puncture below the groin, insert a guide wire through the puncture needle, and then withdraw the puncture needle. Insert a catheter through a guide wire and place it at the target blood vessel, which is the supplying artery of the

tumor lesion, under the guidance of X-ray fluoroscopy or DSA imaging. Exit the guide wire, retain the sheath, and inject chemotherapy drugs through the sheath. Continuously pump chemotherapy within 48–72 h. It should be noted that patients after CIFAC must be absolutely bedridden and their surgical limbs should not be bent. If there are no abnormal conditions, the patient can turn over on both sides within 6 h after surgery. During the turning process, it is necessary to keep the surgical limb from bending. The ankle joint and metacarpophalangeal joint on the surgical side can be moved, but the hip joint can only be moved left and right on the bed (i.e., abduction and adduction movements), and cannot be excessively raised. 4–6 weeks/time, lasting 2–5 times.

Observation items and evaluation criteria

To ensure the homogeneity of data collection, nursing staff in the department reminded patients to come for a follow-up visit via phone on the 7th and 1st day before treatment for 60 and 90 days. Failure to come for a follow-up visit on the 3rd day after the follow-up visit will be considered as giving up participation in this study.

Serum tumor markers (STM)

Prior to treatment, 60d and 90d after treatment, 3 ml of venous blood collected from patients on an empty stomach in the morning is used to isolate the upper layer of serum through the process of settling and centrifugation. Subsequently, enzyme-linked immunosorbent assay is used for detection. The normal range of Golgi protein 73 (GP73) in two groups of patients is 0-18.3 ng/ml; AFP normal value: $\leq 25 \mu g/L$; the normal range of AFP-L3 is 0-20ug/L. Detect indicators such as GP73, AFP, and AFP-L3, and indocyanine green (ICG) excretion test, instruct the patient to fast for 8 h, mix the mold injection water with ICG powder to make a 5 mg/ml solution, assist the patient in lying down and breathing smoothly, use a liver function analyzer and connect the photosensitive probe to the nasal wing, then quickly inject the mixed Rongya through the elbow vein, record the automatic analysis and export ICG 15-minute retention rate (ICG R15), with ICG R15 < 10% indicating normal liver reserve function.

Liver function

Before treatment, 60d and 90d of treatment, 3 ml of fasting venous blood are taken from both groups of patients. After



centrifugation, liver function indicators such as ALT (0-40U/L) and AST (0-40U/L) in the serum are measured.

Adverse reactions

Observe the occurrence of adverse reactions such as nausea, vomiting, bone marrow suppression (BMS), liver pain, and fever in both groups of patients.

Quality of life (QoL)

Evaluate using the Karnofsky scoring scale before treatment, 60 days of treatment, and 90 days of treatment. The total score is 0–100 points, and the higher the score, the better the patient's QoL [27].

Survival rate

Compare the survival status of two groups of patients within one year of treatment.

Statistical methods

Statistical analysis is conducted using SPSS 26.0 software. The measurement data of normal distribution are represented by mean \pm standard deviation ($\overline{x} \pm s$), and t-test is used for inter-group comparison. Count data are expressed in terms of frequency and percentage (%), and inter-group comparisons are made using the x^2 -test. P < 0.05 indicates a statistically significant difference.

Results

Serum tumor markers

In Table 1, STM of the first two groups of patients before treatment: P > 0.05. After 60 and 90 days of treatment, patients in the CIFAC group showed lower GP73, AFP, and AFP-L3 levels than those in the TACE group (P < 0.05) as shown in Fig. 1.

Table 1 STM between two groups after different treatment times $(\bar{x} \pm s)$

Group	GP73 (ng/ml)			AFP (μ g/L)			AFP-L3 (µg/L)		
	Pre- treatment	60d of treatment	90d of treatment	Pre- treatment	60d of treatment	90d of treatment	Pre- treatment	60d of treatment	90d of treatment
CIFAC $(n=54)$	33.75 ± 2.26	17.25 ± 3.74	13.57 ± 1.22	86.61 ± 2.00	24.63 ± 1.46	12.73 ± 3.26	30.46 ± 1.46	23.63 ± 1.72	12.91 ± 1.79
TACE (n=54)	33.72 ± 2.04	18.65 ± 2.27	15.52 ± 2.04	86.40 ± 1.67	26.13 ± 2.03	16.34 ± 1.86	30.64 ± 1.13	24.44 ± 1.16	16.83 ± 2.89
t	0.072	2.352	6.028	0.592	4.408	7.068	0.716	2.869	8.474
p	0.942	0.021	< 0.001	0.555	< 0.001	< 0.001	0.475	0.005	< 0.001

 $\begin{aligned} &\text{GP73: } F_{\text{time}}/P_{\text{time}} = 2002.120, <0.001, F_{\text{inter-group}}/P_{\text{inter-group}} = 17.430, <0.001, F_{\text{timexinter-group}}/P_{\text{timexinter-group}} = 5.010, 0.007; \\ &\text{AFP: } F_{\text{time}}/P_{\text{time}} = 41,700.540, <0.001, F_{\text{inter-group}}/P_{\text{inter-group}} = 32.960, <0.001, F_{\text{timexinter-group}}/P_{\text{timexinter-group}} = 12.960, <0.001; \\ &\text{AFP-L3: } F_{\text{time}}/P_{\text{time}} = 1772.920, <0.001, F_{\text{inter-group}}/P_{\text{inter-group}}/P_{\text{inter-group}}/P_{\text{timexinter-group}}/P_{\text{timexinter-group}} = 21.200, <0.001; \end{aligned}$

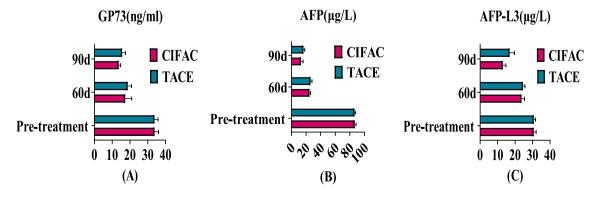


Fig. 1 Color bar chart comparison of STM indicators after different treatment times in patients. *Note*: A shows GP73; B shows AFP; C shows AFP-L3



Liver function

Table 2 presents the comparison of liver function indicators before treatment among patients: P > 0.05. After 60 and 90 days of treatment, patients in the CIFAC group had lower ALT, AST, and ICG15 than those in the TACE group (P < 0.05) as shown in Fig. 2.

Adverse reactions

In Table 3, the incidence of adverse reactions such as nausea, vomiting, BMS, liver pain, and fever in the CIFAC was lower than that in the TACE (P < 0.05) as shown in Fig. 3.

Quality of life

Table 4 presents the comparison of QoL between the two groups before treatment: P > 0.05. After 60 days of treatment

Table 2 Liver function between two groups with different treatment times $[(\bar{x} \pm s)]$

Group	ALT (U/L)			AST (U/L)			CGR15 (%)		
	Pre- treatment	60d of treatment	90d of treatment	Pre- treatment	60d of treatment	90d of treatment	Pre- treatment	60d of treatment	90d of treatment
CIFAC $(n=54)$	65.84 ± 2.23	37.22 ± 4.52	22.46 ± 3.14	64.37 ± 1.34	35.44 ± 6.34	29.19±3.46	31.25 ± 5.12	18.63 ± 3.52	9.02 ± 0.35
TACE (n=54)	65.19 ± 2.36	39.48 ± 3.33	26.13 ± 4.67	64.34 ± 1.24	40.99 ± 4.18	33.56 ± 3.58	31.19 ± 4.89	20.52 ± 3.41	15.36 ± 1.05
t	1.471	2.958	4.792	0.121	5.371	6.450	0.062	2.834	42.094
p	0.144	0.004	< 0.001	0.904	< 0.001	< 0.001	0.950	0.006	0.000

 $\begin{aligned} & \text{ALT: } F_{\text{time}} / P_{\text{time}} = 3817.120, <0.001, F_{\text{inter-group}} / P_{\text{inter-group}} = 20.790, <0.001, F_{\text{time} \times \text{inter-group}} / P_{\text{time} \times \text{inter-group}} = 10.540, <0.001; \\ & \text{AST: } F_{\text{time}} / P_{\text{time}} = 2234.440, <0.001, F_{\text{inter-group}} / P_{\text{inter-group}} = 64.920, <0.001, F_{\text{time} \times \text{inter-group}} / P_{\text{time} \times \text{inter-group}} = 15.900, <0.001; \end{aligned}$

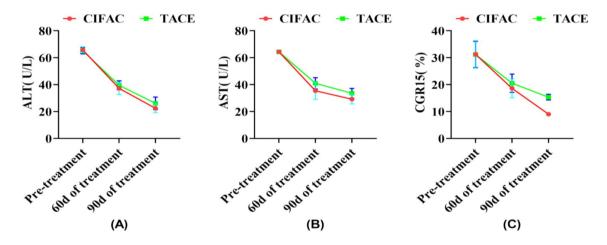


Fig. 2 Comparison of liver function indicators between two groups of patients after different treatment times. *Note*: **A** is ALT; **B** is AST. The closer the filling line is to the center of the circle, the better the liver function recovery

Table 3 Comparison of adverse reactions between two groups (%)

Group	Nausea and vomiting	BMS	Pain in the liver region	Fever	Adverse reaction incidence rate
CIFAC $(n=54)$	1 (1.85)	0 (0.00)	0 (0.00)	0 (0.00)	1 (1.85)
TACE $(n=54)$	2 (3.70)	2 (3.70)	2 (3.70)	2 (3.70)	8 (14.82)
X^2	_	_	_	_	5.939
p	_	_	_	_	0.015



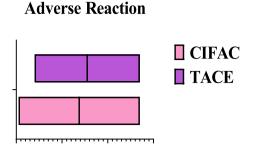


Fig. 3 Box plot comparison of adverse reactions in both groups. *Note*: The vertical axis represents groups, represented by different colors or markings; the horizontal axis represents the percentage or frequency of adverse reactions in patients, and the scale on the horizontal axis should reflect this data range

60

40

20

0

Table 4 Comparison of QoL scores between two groups after different treatment times $[(\bar{x} \pm s), score]$

Group	KPS					
	Pre-treatment	60d of treatment	90d of treatment			
CIFAC $(n=54)$	48.20±4.96	67.19 ± 6.97	72.63 ± 5.53			
TACE $(n=54)$	47.83 ± 5.79	57.87 ± 5.27	63.72 ± 7.33			
t	0.357	7.838	7.131			
p	0.722	< 0.001	< 0.001			

$$\begin{split} & \text{KPS: } F_{\text{time}}/P_{\textit{time}} = 363.310, <0.001, \ F_{\text{inter-group}}/P_{\text{inter-group}} = 68.770, <0.\\ & 001, \ F_{\text{time}\times\text{inter-group}}/P_{\text{time}\times\text{inter-group}} = 21.340, <0.001; \end{split}$$

and 90 days of treatment, the Karnofsky score of patients in the CIFAC group was higher than that in the TACE group (P < 0.05), as shown in Fig. 4.

Survival rate comparison

The one-year survival rate of 33 cases (61.11%) in the CIFAC group was significantly higher than that of 23 cases (42.59%) in the TACE group (P < 0.05) (Fig. 5).

Discussion

This article found through analysis that CIFAC improves STM levels in liver cancer patients (P < 0.05). CIFAC is a treatment method for liver cancer, whose main purpose is to deliver chemotherapy drugs directly to the tumor site of the liver through a catheter, in order to increase the concentration of drugs in tumor tissue, enhance chemotherapy efficacy, and reduce damage to normal tissue [28]. Chemotherapy drugs are directly delivered to the tumor site through the femoral artery catheter and

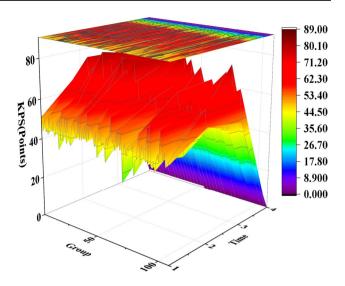


Fig. 4 Comparison of 3D color mapping surface projection maps of QoL scores for patients at different treatment times. *Note*: The X-axis and Y-axis represent the treatment time, representing pretreatment, 60 days, and 90 days; The Z-axis is the QoL score, which is usually a value between 0 and 100 or other ranges, with higher values indicating better QoL. Color mapping: The colors in the graph represent the specific values of the QoL score, blue may represent lower scores, and red may represent higher scores. Surface projection: Through a 3D surface, the trend of changes in the QoL scores of two groups of patients can be seen over time. The undulations and height changes of the surface can intuitively reflect the fluctuations and trends of the score

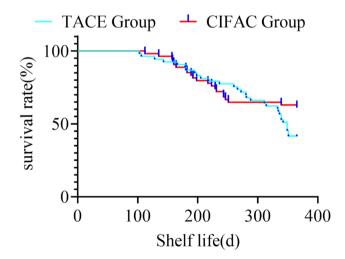


Fig. 5 1-year survival curves of two groups of patients treated differently

continuously perfused, forming a high concentration drug environment locally, directly killing tumor cells (TCs) or inhibiting their growth [29]. When TCs are killed or their growth is inhibited, the production of tumor markers like GP73, AFP, and AFP-L3 decreases, leading to a decrease in serum levels of tumor markers [30]. Chemotherapy drugs



can induce tumor cell apoptosis, which is the process of tumor cell self-destruction [31]. An increase in the number of apoptotic TCs can lead to a decrease in the production of tumor markers, thereby lowering STM levels [32]. It can also inhibit the generation of tumor neovascularization, thereby blocking the nutritional and oxygen supply of TCs [33]. This can lead to inhibition or death of tumor cell growth, thereby reducing the production of tumor markers [34]. In terms of pathological mechanisms, the increase of STM levels such as GP73, AFP, and AFP-L3 in liver cancer patients is related to factors such as tumor cell proliferation, abnormal differentiation, and blocked apoptosis [35]. Continuous infusion chemotherapy can improve these pathological processes by directly killing TCs, inducing tumor cell apoptosis, and inhibiting tumor neovascularization, thereby reducing STM levels [36].

The research demonstrated that the liver function level of patients in the CIFAC was significantly improved (P < 0.05). ALT is mainly present in tissues and cells such as the liver, heart, and skeletal muscle, especially in the liver [37]. When these tissue cells, especially liver cells, are damaged, the release of ALT increases, leading to an increase in ALT activity after entering the bloodstream [38]. The degree of ALT elevation is directly proportional to the degree of liver cell damage, making it a sensitive marker of acute liver cell damage and an important indicator for diagnosing viral and toxic hepatitis [39]. AST is mainly present in human myocardial cells, followed by tissues such as liver, kidney, and skeletal muscle [40]. Under normal circumstances, the content of aspartate aminotransferase in human serum is relatively low. However, when cells such as the myocardium, liver, kidneys, or skeletal muscles are damaged or destroyed, the permeability of the cell membrane increases, leading to the release of intracellular aspartate aminotransferase into the bloodstream, resulting in a significant increase in serum aspartate aminotransferase levels [41]. Through femoral artery catheterization, chemotherapy drugs can be directly delivered to the liver region where the tumor is located, allowing the drug to reach a higher concentration in the tumor tissue, thereby enhancing its killing effect on TCs [42]. CIFAC can slowly release drugs in the liver, avoiding the rapid metabolism and excretion of drugs in the body in traditional chemotherapy methods, thereby reducing the damage and side effects of drugs on normal tissues [43]. Chemotherapy drugs not only kill TCs, but also cause certain damage to normal liver cells. However, CIFAC can reduce damage to liver cells by reducing drug dosage and concentration, thereby contributing to the recovery of liver function [44]. For infusion chemotherapy via femoral artery catheterization, chemotherapy drugs can be directly delivered to the blood supply artery of liver cancer, increasing local drug concentration and enhancing the killing effect on liver cancer cells. The metabolism

of indocyanine green in the liver is closely related to the functional status of the liver. After tumor cells are killed, liver function may be improved to a certain extent, thereby affecting the ICG15 retention rate and making it tend toward normalization. In addition, infusion chemotherapy through femoral artery catheterization can improve the overall blood circulation of the liver. Good blood supply helps liver cells obtain more oxygen and nutrients, enhance the metabolic capacity of liver cells, and the high metabolic state of the liver may affect the metabolic pathways of ICG, altering the 15 min retention rate of ICG [45].

The results showed a significant decrease in adverse reactions among patients in the CIFAC group (P < 0.05). Through femoral artery catheterization, chemotherapy drugs can be directly delivered to the tumor site of the liver, increasing the concentration of drugs in the tumor tissue, thereby improving the effectiveness of chemotherapy and reducing the incidence of systemic adverse reactions [46]. CIFAC can maintain a stable concentration of drugs in the liver, avoiding fluctuations in drug concentration in traditional chemotherapy methods, thereby reducing drug damage to normal tissues and reducing the occurrence of adverse reactions [47]. CIFAC can reduce the toxic side effects of chemotherapy drugs on other organs in the body, such as BMS, nausea and vomiting [48]. This is because drugs mainly pass through local perfusion, reducing the circulation and metabolism of drugs in the body, thereby reducing the toxic side effects of drugs on the whole body [49]. By reducing the occurrence of adverse reactions like nausea, vomiting, and BMS, CIFAC can improve the QoL of patients and maintain good physical and mental states during the treatment process [50].

In addition, the study also found that the quality of life and 1-year survival rate of patients undergoing continuous infusion chemotherapy via femoral artery catheterization were significantly improved (P < 0.05). Through femoral artery catheterization, chemotherapy drugs can be directly delivered to the liver tumor site, achieving precise drug delivery [51]. This approach can ensure that the drug reaches a high concentration in tumor tissue, thereby improving chemotherapy efficacy [52]. CIFAC can enable drugs to continue to exert their effects at the tumor site, avoiding the problem of drug concentration fluctuations in traditional chemotherapy methods, helping to maintain stable chemotherapy efficacy, and reducing the risk of tumor recurrence [53]. CIFAC can reduce the damage of drugs to other normal tissues, reduce the side effects caused by chemotherapy, improve the QoL of patients, and reduce the pain during the treatment process [54].



Conclusion

In summary, CIFAC is a highly targeted method for treating liver cancer, which involves placing a catheter in the femoral artery to deliver chemotherapy drugs directly to the liver tumor site. Drugs can generate high concentrations and longterm exposure locally, thereby achieving precise targeting of TCs. In addition, this treatment method can also improve the liver function of patients, reduce adverse reactions during chemotherapy, and improve their QoL and survival. During the treatment process, chemotherapy drugs directly act on the tumor site, which can kill TCs and reduce the damage of drugs to normal cells. This is because the concentration of chemotherapy drugs in tumor tissue is higher than in other parts of the body, thus achieving targeted treatment of tumors. At the same time, this method can also alleviate the patient's pain, alleviate the progression of the condition, and buy more treatment time for the patient. However, there is research on long-term efficacy in this study, which makes it necessary for the study to be complete. It is hoped that clinical scholars can expand their research based on this study in the future.

Author contributions Qiong Yan and Xinguo Sun were involved in conceptualization and writing—original draft. Yubo Wang and Shijiao Duan were responsible for methodology, investigation, and data curation. Bo Wang took part in writing—reviewing and editing. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Funding The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Affiliated Nanhua Hospital. Informed consent was obtained from participants to participate in the study.

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's

Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

References

- Cheng K, Cai N, Zhu J, Yang X, Liang H, Zhang W. Tumorassociated macrophages in liver cancer: From mechanisms to therapy. Cancer Commun. 2022;42(11):1112–40. https://doi.org/ 10.1002/cac2.12345.
- Li X, Ramadori P, Pfister D, Seehawer M, Zender L, Heikenwalder M. The immunological and metabolic landscape in primary and metastatic liver cancer. Nat Rev Cancer. 2021;21(9):541-57. https://doi.org/10.1038/ s41568-021-00383-9.
- Wang W, Wang C, Xu H, Gao Y. Aldehyde dehydrogenase, liver disease and cancer. Int J Biol Sci. 2020;16(6):921–34. https:// doi.org/10.7150/ijbs.42300.
- 4. Yang WS, Zeng XF, Liu ZN, Zhao QH, Tan YT, Gao J, et al. Diet and liver cancer risk: a narrative review of epidemiological evidence. Br J Nutr. 2020;124(3):330–40. https://doi.org/10.1017/S0007114520001208.
- Maki H, Hasegawa K. Advances in the surgical treatment of liver cancer. Biosci Trends. 2022;16(3):178–88. https://doi.org/ 10.5582/bst.2022.01245.
- Korean Liver Cancer Association (KLCA) and National Cancer Center (NCC) Korea. 2022 KLCA-NCC Korea practice guidelines for the management of hepatocellular carcinoma. Clin Mol Hepatol 2022;28(4):583–705. https://doi.org/10.3350/ cmh.2022.0294.
- Alannan M, Fayyad-Kazan H, Trézéguet V, Merched A. Targeting lipid metabolism in liver cancer. Biochemistry. 2020;59(41):3951– 64. https://doi.org/10.1021/acs.biochem.0c00477.
- Affo S, Filliol A, Gores GJ, Schwabe RF. Fibroblasts in liver cancer: functions and therapeutic translation. Lancet Gastroenterol Hepatol. 2023;8(8):748–59. https://doi.org/10.1016/S2468-1253(23)00111-5.
- Shi JF, Cao M, Wang Y, Bai FZ, Lei L, Peng J, et al. Is it possible to halve the incidence of liver cancer in China by 2050? Int J Cancer. 2021;148(5):1051–65. https://doi.org/10.1002/ijc.33313.
- Gao S, Gang J, Yu M, Xin G, Tan H. Computational analysis for identification of early diagnostic biomarkers and prognostic biomarkers of liver cancer based on GEO and TCGA databases and studies on pathways and biological functions affecting the survival time of liver cancer. BMC Cancer. 2021;21(1):791. https://doi.org/10.1186/s12885-021-08520-1.
- Huan HB, Chen XJ, Xia F. Liver cancer immunotherapy in the context of precision medicine. Zhonghua Gan Zang Bing Za Zhi. 2020;28(11):910–4. https://doi.org/10.3760/cma.j.cn501113-20201029-00585. (Chinese).
- Zhao K, Zhou X, Xiao Y, Wang Y, Wen L. Research progress in alpha-fetoprotein-induced immunosuppression of liver cancer. Mini Rev Med Chem. 2022;22(17):2237–43. https://doi.org/10. 2174/1389557522666220218124816.
- Xu H, Yuan Q, Wu Z, Xu Y, Chen J. Integrative transcriptome and single-cell sequencing technology analysis of the potential therapeutic benefits of oleanolic acid in liver injury and liver cancer. Aging. 2023;15(24):15267–86. https://doi.org/10.18632/ aging.205349.
- He L, Peng X, Chen N, Wei Z, Wang J, Liu Y, et al. Automated treatment planning for liver cancer stereotactic body radiotherapy.



- Clin Transl Oncol. 2023;25(11):3230–40. https://doi.org/10.1007/s12094-023-03196-4.
- Singal AG, Sanduzzi-Zamparelli M, Nahon P, Ronot M, Hoshida Y, Rich N, et al. International Liver Cancer Association (ILCA) white paper on hepatocellular carcinoma risk stratification and surveillance. J Hepatol. 2023;79(1):226–39. https://doi.org/10. 1016/j.jhep.2023.02.022.
- Gillman R, Lopes Floro K, Wankell M, Hebbard L. The role of DNA damage and repair in liver cancer. Biochim Biophys Acta Rev Cancer. 2021;1875(1): 188493. https://doi.org/10.1016/j. bbcan.2020.188493.
- Zhang Z, Hui L. Progress in patient-derived liver cancer cell models: a step forward for precision medicine. Acta Biochim Biophys Sin. 2023;55(11):1707–17. https://doi.org/10.3724/abbs. 2023224.
- Li K, Sun H, Wu CX. Research progress of compound injection of traditional Chinese medicine in the treatment of liver cancer. Zhonghua Gan Zang Bing Za Zhi. 2022;30(9):1007–11. https://doi.org/10.3760/cma.j.cn501113-20210927-00486. (Chinese).
- Speciale A, Muscara C, Molonia MS, Cristani M, Cimino F, Saija A. Recent advances in glycyrrhetinic acid-functionalized biomaterials for liver cancer-targeting therapy. Molecules. 2022;27(6):1775. https://doi.org/10.3390/molecules27061775.
- Naar L, Hatzaras I. Liver resection for hepatocellular carcinoma and the barcelona clinic liver cancer criteria: is it time to push the limits? Ann Surg Oncol. 2020;27(7):2122–4. https://doi.org/10. 1245/s10434-020-08459-w.
- Liu YC, Yeh CT, Lin KH. Cancer stem cell functions in hepatocellular carcinoma and comprehensive therapeutic strategies. Cells. 2020;9(6):1331. https://doi.org/10.3390/cells 9061331
- Wege H, Schulze K, von Felden J, Calderaro J, Reig M. Rare liver tumors working group of the European Reference Network on Hepatological Diseases (ERN RARE-LIVER). Rare variants of primary liver cancer: Fibrolamellar, combined, and sarcomatoid hepatocellular carcinomas. Eur J Med Genet. 2021;64(11):104313. https://doi.org/10.1016/j.ejmg.2021.104313.
- Chen K, Yang F, Zhu X, Qiao G, Zhang C, Tao J, et al. Association between pro-inflammatory diet and liver cancer risk: a systematic review and meta-analysis. Public Health Nutr. 2023;26(12):2780– 9. https://doi.org/10.1017/S1368980023002574.
- Mostafaei F, Mahdinloo S, Valizadeh H, Hemmati S, Abdi M, Sarfraz M, et al. An update review of smart nanotherapeutics and liver cancer: opportunities and challenges. Nanomedicine. 2023;18(25):1855–73. https://doi.org/10.2217/nnm-2023-0196.
- Fu X, Zhang Y, Luo Q, Ju Y, Song G. Targeting the mechanomicroenvironment and liver cancer stem cells: a promising therapeutic strategy for liver cancer. Cancer Biol Med. 2023;20(11):816–29. https://doi.org/10.20892/j.issn.2095-3941. 2023.0229.
- Seo JY, Shin DW, Yu SJ, Jung JH, Han K, Cho IY, et al. Disparities in liver cancer surveillance among people with disabilities: a national database study in Korea. J Clin Gastroenterol. 2021;55(5):439–48. https://doi.org/10.1097/MCG.0000000000 001405.
- Romano F, Chiarelli M, Garancini M, Scotti M, Zago M, Cioffi G, et al. Rethinking the Barcelona clinic liver cancer guidelines: intermediate stage and Child-Pugh B patients are suitable for surgery? World J Gastroenterol. 2021;27(21):2784–94. https://doi.org/10.3748/wjg.v27.i21.2784.
- Huang PS, Wang LY, Wang YW, Tsai MM, Lin TK, Liao CJ, et al. Evaluation and application of drug resistance by biomarkers in the clinical treatment of liver cancer. Cells. 2023;12(6):869. https:// doi.org/10.3390/cells12060869.

- Korean Liver Cancer Association (KLCA); National Cancer Center (NCC), Goyang, Korea. 2018 Korean Liver Cancer Association-National Cancer Center Korea Practice Guidelines for the Management of Hepatocellular Carcinoma. Korean J Radiol 2019;20(7):1042–1113. https://doi.org/10.3348/kjr.2019.0140.
- Fatma H, Siddique HR. Pluripotency inducing Yamanaka factors: role in stemness and chemoresistance of liver cancer. Expert Rev Anticancer Ther. 2021;21(8):853–64. https://doi.org/10.1080/ 14737140.2021.1915137.
- Krstić MN, Mijač D, Tomašević RS, Lukić S, Stojković Lalošević M, Krstić JM, et al. Abnormal liver blood tests: hepatologist approach. Dig Dis. 2022;40(2):206–14. https://doi.org/10.1159/ 000517110.
- 32. Ataei A, Deng J, Muhammad W. Liver cancer risk quantification through an artificial neural network based on personal health data. Acta Oncol. 2023;62(5):495–502. https://doi.org/10.1080/0284186X.2023.2213445.
- Cao JJ, Kwon DH, Ghaziani TT, Kwo P, Tse G, Kesselman A, et al. Accuracy of information provided by ChatGPT regarding liver cancer surveillance and diagnosis. AJR Am J Roentgenol. 2023;221(4):556–9. https://doi.org/10.2214/AJR.23.29493.
- 34. Cheng X, Chen JZ, Guo YB. Regulatory effect of molecular targeted drugs on the immune system for liver cancer. Zhonghua Gan Zang Bing Za Zhi. 2021;29(10):1031–4. https://doi.org/10.3760/cma.j.cn501113-20191006-00363. (Chinese).
- Tsilimigras DI, Aziz H, Pawlik TM. Critical analysis of the updated barcelona clinic liver cancer (BCLC) Group Guidelines. Ann Surg Oncol. 2022;29(12):7231–4. https://doi.org/10.1245/ s10434-022-12242-4.
- 36. Rim CH, Lee WJ, Musaev B, Volichevich TY, Pazlitdinovich ZY, Nigmatovich TM, et al. Consortium of Republican Specialized Scientific Practical-Medical Center of Oncology and Radiology and South Korean Oncology Advisory Group. Challenges and suggestions in management of lung and liver cancer in Uzbekistan: the second report of the Uzbekistan-Korea Oncology Consortium. Int J Environ Res Public Health. 2022;19(18):11727. https://doi.org/10.3390/ijerph191811727.
- 37. Heinrich S, Craig AJ, Ma L, Heinrich B, Greten TF, Wang XW. Understanding tumour cell heterogeneity and its implication for immunotherapy in liver cancer using single-cell analysis. J Hepatol. 2021;74(3):700–15. https://doi.org/10.1016/j.jhep.2020. 11.036.
- Cheng Z, Wei-Qi J, Jin D. New insights on sorafenib resistance in liver cancer with correlation of individualized therapy. Biochim Biophys Acta Rev Cancer. 2020;1874(1): 188382. https://doi.org/ 10.1016/j.bbcan.2020.188382.
- 39. Li X, Li C, Zhang L, Wu M, Cao K, Jiang F, et al. The significance of exosomes in the development and treatment of hepatocellular carcinoma. Mol Cancer. 2020;19(1):1. https://doi.org/10.1186/s12943-019-1085-0.
- 40. George J, Kawaguchi T. Liver fat and a perturbed metabolic milieu: a consilience of factors driving liver cancer development. Hepatol Int. 2022;16(4):733–6. https://doi.org/10.1007/s12072-022-10352-5.
- Lee IJ, Chun HJ, Chung JW. 2022 Korean liver cancer associationnational cancer center korea practice guidelines for transarterial therapy of hepatocellular carcinoma: what's new? Korean J Radiol. 2023;24(1):6–9. https://doi.org/10.3348/kjr.2022.0510.
- 42. Selby LV, Ejaz A, Brethauer SA, Pawlik TM. Fatty liver disease and primary liver cancer: disease mechanisms, emerging therapies and the role of bariatric surgery. Expert Opin Investig Drugs. 2020;29(2):107–10. https://doi.org/10.1080/13543784.2020. 1721457.
- Han Q, Du L, Zhu L, Yu D. Review of the application of dual drug delivery nanotheranostic agents in the diagnosis and treatment



- of liver cancer. Molecules. 2023;28(20):7004. https://doi.org/10.3390/molecules28207004.
- Qu H, Liu J, Zhang D, Xie R, Wang L, Hong J. Glycolysis in chronic liver diseases: mechanistic insights and therapeutic opportunities. Cells. 2023;12(15):1930. https://doi.org/10.3390/ cells12151930.
- Tan DJH, Setiawan VW, Ng CH, Lim WH, Muthiah MD, Tan EX, et al. Global burden of liver cancer in males and females: changing etiological basis and the growing contribution of NASH. Hepatology. 2023;77(4):1150–63. https://doi.org/10.1002/hep. 32758
- Jia JM, Ren JS, Zhang LY. Current status and treatment strategies for liver injury before targeted immunotherapy for liver cancer. Zhonghua Gan Zang Bing Za Zhi. 2023;31(11):1133–6. https://doi.org/10.3760/cma.j.cn501113-20230914-00107. (Chinese).
- Inoue M, Tsugane S. Coffee drinking and reduced risk of liver cancer: update on epidemiological findings and potential mechanisms. Curr Nutr Rep. 2019;8(3):182–6. https://doi.org/ 10.1007/s13668-019-0274-1.
- 48. Sariyar E, Firtina KZ. Modelling the sorafenib-resistant liver cancer microenvironment by using 3-D spheroids. Altern Lab Anim. 2023;51(5):301–12. https://doi.org/10.1177/0261192923 1193421.
- Koh E, Kim Y. Risk association of liver cancer and hepatitis b with tree ensemble and lifestyle features. Int J Environ Res Public Health. 2022;19(22):15171. https://doi.org/10.3390/ijerph1922 15171.

- Messaoudi R, Jaziri F, Mtibaa A, Grand-Brochier M, Ali HM, Amouri A, et al. Ontology-based approach for liver cancer diagnosis and treatment. J Digit Imaging. 2019;32(1):116–30. https://doi.org/10.1007/s10278-018-0115-6.
- Mauro E, Forner A. Barcelona clinic liver cancer 2022 update: Linking prognosis prediction and evidence-based treatment recommendation with multidisciplinary clinical decision-making. Liver Int. 2022;42(3):488–91. https://doi.org/10.1111/liv.15180.
- 52. Lin HY, Li CJ, Yang YL, Huang YH, Hsiau YT, Chu PY. Roles of lysyl oxidase family members in the tumor microenvironment and progression of liver cancer. Int J Mol Sci. 2020;21(24):9751. https://doi.org/10.3390/ijms21249751.
- Yu M, Li S. Irreversible electroporation for liver cancer ablation: a meta analysis. Eur J Surg Oncol. 2022;48(6):1321–30. https://doi.org/10.1016/j.ejso.2021.12.015.
- Lin ZZ, Xu YC, Liu CX, Lu XL, Wen FY. Physical activity and liver cancer risk: a systematic review and meta-analyses. Clin J Sport Med. 2021;31(1):86–90. https://doi.org/10.1097/JSM.00000 00000000689.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

