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ORIGINAL RESEARCH

# Hepatic Arterial Infusion Chemotherapy Combined Apatinib/Camrelizumab for Recurrent Hepatocellular Carcinoma After Hepatectomy

Xin Zheng[1], Kun Qian[2,3]

[1]Department of Hepatopancreatobiliary Surgery, The First College of Clinical Medical Science, China Three Gorges University & Yichang Central People's Hospital, Yichang, People's Republic of China; [2]Department of Radiology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430022, People's Republic of China; [3]Hubei Provincial Clinical Research Center for Precision Radiology & Interventional Medicine, Wuhan, 430022, People's Republic of China

Correspondence: Kun Qian, Department of Radiology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430022, People's Republic of China, Email kunchien@163.com



**Background:** This study aimed to assess the efficacy and safety of hepatic arterial infusion chemotherapy (HAIC) combined with apatinib and camrelizumab in patients with recurrent hepatocellular carcinoma (HCC) following hepatectomy.

**Methods:** From July 2020 to December 2024, consecutive medical records of recurrent HCC patients treated with HAIC plus apatinib/camrelizumab were retrospectively reviewed. Key outcomes, including overall survival (OS), progression-free survival (PFS), therapeutic response, and treatment-related complications, were evaluated.

**Results:** The study was followed up until January 31, 2025, with a median follow-up duration of 11 months (range: 2–26 months). Among the 110 eligible recurrent HCC patients (91 males and 19 females), 62 deaths were recorded. The objective response rate (ORR) was 31.8%, and the disease control rate (DCR) was 87.3%. The median OS was 14 months (95% CI: 12.9–15.1 months), with multivariable analysis identifying vascular invasion as an independent prognostic factor for OS. The median PFS was 7 months (95% CI: 5.3–8.7 months), and the platelet-to-lymphocyte ratio was found to be an independent prognostic factor for PFS. All adverse events were manageable, and no treatment-related deaths occurred.

**Conclusion:** HAIC combined with apatinib/camrelizumab is effective and safe in the treatment of recurrent HCC after hepatectomy, which may be a promising treatment for recurrent HCC.

**Keywords:** hepatic arterial infusion chemotherapy, apatinib, camrelizumab, hepatocellular carcinoma, recurrent

## Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver cancer and the third leading cause of cancer death worldwide.[1] While hepatectomy and liver transplantation offer curative potential for early-stage HCC, most patients present with advanced disease requiring systemic therapies.[2] However, tumor recurrence after resection is a difficult problem in the treatment of HCC, which seriously affects the prognosis of patients. The reported data indicates that HCC patients experience a high rate of tumor recurrence, with 50% to 70% recurring within 5 years post-surgery and 61.4% to 83.3% recurring within 2 years. Additionally, the overall survival (OS) rates for recurrent HCC patients are 81.1% at 1 year and 60.7% at 5 years, compared to significantly higher rates of 95.8% and 92.9% for patients without recurrence, respectively.[3,4] Currently, there is still a lack of unified standards for the treatment of recurrent tumors, and re-surgical resection may be an effective treatment, but the patient's liver reserve function and willingness make it impossible. Hence, it is of great value to explore other effective treatment methods to control the residual tumor for improving the prognosis of recurrent HCC patients.

Recent advancements in systematic therapies, particularly molecular targeted agents (MTAs) and immune checkpoint inhibitors (ICIs), have significantly progressed the treatment of HCC. However, tumor heterogeneity and complex

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microenvironment interactions, including iron dysregulation[5] and immune cell infiltration patterns,[6] continue to pose significant therapeutic challenges. According to the NCCN Clinical Practice Guidelines in Hepatobiliary Cancers, the combination of atezolizumab and bevacizumab has been established as the first-line therapy for HCC, marking the onset of the immunological era in first-line treatment for advanced HCC.[7] Additionally, apatinib, a novel vascular endothelial growth factor receptor-2 inhibitor, has demonstrated promising antitumor efficacy and manageable toxicity in HCC treatment.[8] Furthermore, camrelizumab, an anti-PD-1 monoclonal antibody, has been approved in China as a second-line therapy for unresectable HCC. Studies by Xu et al have revealed that the combination of apatinib and camrelizumab exhibits encouraging clinical activity in patients with advanced HCC.[9]

Hepatic arterial infusion chemotherapy (HAIC), as a kind of local interventional therapy, has developed into a promising therapeutic method by increasing the concentration of local chemotherapy drugs in tumor tissue, improving tumor response rate and reducing systemic toxicity.[10,11] Tumors characterized by a low mutation burden and fewer neoantigens typically exhibit reduced immunogenicity, resulting in limited responsiveness to immunotherapy. However, combining locoregional therapies can not only decrease the overall tumor burden but also enhance the release of neoantigens. This process facilitates lymphocyte infiltration into tumor tissues, alleviates the immunosuppressive tumor microenvironment, and ultimately strengthens the immune response.[12,13] Notably, hepatic arterial infusion chemotherapy (HAIC) has been reported to effectively reduce intrahepatic tumor burden and stimulate the exposure of tumor neoantigens, thereby enhancing the efficacy of targeted and immunotherapeutic approaches.[14] Hence, HAIC combined with apatinib/camrelizumab may have synergistic and positive effects for the treatment of recurrent HCC.

However, there is limited research on the triple therapy approach combining HAIC with apatinib and camrelizumab for recurrent HCC following hepatectomy. Consequently, this retrospective study aims to assess the efficacy and safety of HAIC in combination with apatinib and camrelizumab for the treatment of recurrent HCC.

# Methods

## Selection of Patients

From July 2020 to December 2024, 131 recurrent HCC patients after hepatectomy received HAIC+apatinib+camrelizumab in our medical center. HCC was diagnosed according to the diagnostic criteria of the European Association for the Study of Liver and the American Association for the Study of Liver Disease. Treatment regimens for all patients were nominated by the multidisciplinary tumor board.

The inclusion criteria for patient selection were as follows: (1) patients diagnosed with recurrent HCC; (2) Child-Pugh class A or B without the presence of ascites; and (3) an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. The exclusion criteria included: (1) prior treatment with anti-angiogenesis therapy, ICIs, or TACE; (2) hepatic dysfunction or renal impairment; (3) receipt of additional treatments such as radiofrequency ablation or iodine-125 seed implantation alongside HAIC during the study period; (4) a history of malignancies other than HCC; and (5) loss to follow-up.

This retrospective study was conducted in accordance with the principles of the Declaration of Helsinki. The present study was approved by the Ethics Committee of Wuhan Union Hospital, Tongji Medical College, Huazhong university of Science and Technology. Written informed consent was obtained from all patients.

## Haic

The HAIC procedure was performed according to our institutional standard protocol. First, the femoral artery was punctured with the Seldinger technique after local anesthesia, followed by celiac trunk, mesenteric artery and common hepatic artery angiography with a 5F-Yashiro catheter under digital subtraction angiography. Read the branches of the intrahepatic artery carefully, and embolize the right gastric artery, left gastric artery and other arteries supplying the stomach with coils if they are present. Embolization of the left (right) hepatic artery was sometimes performed to restrict the chemotherapy drug to the right (left) hepatic artery. The microcatheter was placed in the tumor supplying artery. Then, the patient returned to the ward for infusion chemotherapy. The pipe orifice of the catheter was connected to the artery infusion pump to administer the following chemotherapeutic agents: oxaliplatin at 85 mg/m2 for 2–4 h, leucovorin

at 400 mg/m2 for 2h, fluorouracil at 400 mg/m2 for 1 h, and another fluorouracil at 2,400 mg/m2 for more than 46 h. Patients were treated with HAIC every 3 weeks until complete tumor response. In addition, 10mg of dexamethasone was given intravenously in patients undergoing HAIC for the first time to prevent allergy to chemotherapy drugs. However, HAIC therapy should be discontinued under the following circumstances: if the patient cannot tolerate HAIC (eg, severe abdominal pain or nausea and refuses further treatment), if the tumor shows continuous progression, if liver function deteriorates persistently (eg, Child-Pugh class C), or if the patient's performance status declines (eg, ECOG score $\geq 2$). In such cases, HAIC treatment should be interrupted.

### Apatinib/Camrelizuma

Apatinib (250 mg once daily) and camrelizumab were initiated at 3–5 days after HAIC, and the drug dose was given according to the minimum clinically recommended dose. Patients received camrelizumab (200 mg) every 3 weeks, and the drug was interrupted or discontinued if the patient had serious adverse events (AEs). Similarly, apatinib will be discontinued if the patient has a grade 4 or higher AEs (according to Common Terminology Criteria for Adverse Events, Version 5.0). For patients who required multiple HAIC procedures, the apatinibs were withdrawn 2 days before HAIC and resumed 3–5 days after HAIC.

### Definition and Data Evaluation

Following combination therapy, patients underwent contrast-enhanced CT or MRI scans at 6-week intervals for follow-up. Tumor response was assessed using the modified Response Evaluation Criteria in Solid Tumors (mRECIST). The objective response rate (ORR) was defined as the sum of complete response (CR) and partial response (PR), while the disease control rate (DCR) included CR, PR, and stable disease (SD). AEs were documented and evaluated according to the Common Terminology Criteria for Adverse Events (CTCAE, Version 5.0).

### Statistical Analysis

Discrete variables were presented as numbers with percentages, while quantitative data were expressed as mean ± standard deviation. OS and PFS were analyzed using the Kaplan-Meier method. The 95% confidence interval (CI) was calculated for median OS, PFS, and hazard ratio (HR). Univariate analysis was performed using the Log rank test, with variables showing a $P$ value $< 0.10$ included in the multivariate analysis. Potential prognostic factors influencing OS and PFS were evaluated using a Cox proportional hazards regression model. All statistical tests were two-tailed, with $P < 0.05$ considered statistically significant. Data analysis was conducted using SPSS software, Version 24.0 (IBM, Armonk, New York).

## Results

### Study Population

Between July 2020 and December 2024, a total of 110 patients with recurrent HCC were included in this study (Figure 1). The cohort comprised 91 males and 19 females, with a mean age of 55.4 ± 10.9 years. Additional baseline characteristics of the recurrent HCC patients are detailed in Table 1. The study was followed up until January 31, 2025, with a median follow-up duration of 11 months (range: 2–26 months). During this period, 62 patients died. The images of representative patients before and after treatment are shown in Figure 2.

### Treatment Response

Tumor response was evaluated using abdominal contrast-enhanced CT/MR 4 weeks after the initial HAIC. In this study, 3 patients (2.7%) achieved CR, 32 patients (29.1%) achieved PR, and 61 patients (55.5%) achieved SD. Consequently, the ORR was 31.8%, and the DCR was 87.3%.

### Overall Survival

The median OS in this study was 14 months (95% CI: 12.9–15.1 months) (Figure 3). Univariate analysis revealed that tumor size, tumor number, vascular invasion, platelet-to-lymphocyte ratio (PLR), and neutrophil-to-lymphocyte ratio

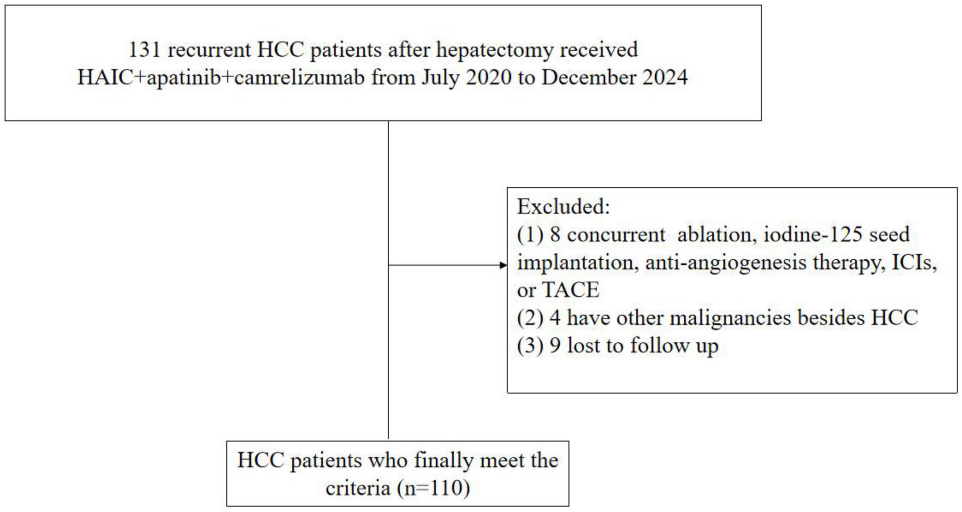


**Figure 1** Flow chart shows the screening procedure for recurrent hepatocellular carcinoma after hepatectomy.

(NLR) were significantly associated with patients' OS (Table 2). When these factors were incorporated into multivariate analysis, vascular invasion emerged as an independent prognostic factor influencing patients' OS ($P$<0.05) (Table 3).

## Pfs

The median PFS was 7 months (95% CI, 5.3 to 8.7 months), as illustrated in Figure 4. Univariate analysis identified tumor number, PLR, and NLR as factors associated with PFS. Furthermore, multivariate analysis revealed that PLR was an independent prognostic factor influencing PFS ($P$<0.05) (Table 4).

**Table 1** Baseline Patient Characteristics

| Characteristic | No, %; Mean ± SD |
|---|---|
| **Gender** | |
| Male | 91 (82.7%) |
| Female | 19 (17.3%) |
| **Age (y)** | 55.4±10.9 |
| **ECOG** | |
| 0 | 44 (40.0%) |
| 1 | 66 (60.0%) |
| Hepatitis B | |
| Yes | 78 (70.9%) |
| No | 32 (29.1%) |
| **Child-Pugh score** | |
| A | 62 (56.4%) |
| B | 48 (43.6%) |
| **α-Fetoprotein level** | |
| >400 ng/mL | 59 (53.6%) |
| ≤400 ng/mL | 51 (46.4%) |
| **Extrahepatic metastases** | |
| Yes | 61 (55.5%) |
| No | 49 (44.5%) |

(*Continued*)

**Table 1** (Continued).

| Characteristic | No, %; Mean ± SD |
|---|---|
| **Largest diameter of tumor (cm)** | 8.5±4.2 |
| **Tumor number** | |
| ≥3 | 91 (82.7%) |
| <3 | 19 (17.3%) |
| **Vascular invasion** | |
| Present | 68 (61.8%) |
| Absent | 42 (38.2%) |
| **Baseline laboratory test result** | |
| Total bilirubin level (μmol/L) | 18.2±9.2 |
| Albumin (g/L) | 34.5±5.2 |
| PT(s) | 14.0±1.6 |
| AST (μmol/L) | 71.9±52.6 |
| ALT (μmol/L) | 47.4±29.8 |
| PLR | 145.5±88.8 |
| NLR | 3.5±2.7 |

**Abbreviations**: SD, Standard deviation; HR, Hazard ratio; CI, Confidence interval; ECOG, Eastern Cooperative Oncology Group; PT, Prothrombin time; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; PLR, Platelet-to-lymphocyte ratio; NLR, Neutrophil-to-lymphocyte ratio.

## Adverse Events

Eighty-two patients (74.5%) experienced abdominal pain of varying degrees at least once during HAIC treatment. The pain symptoms were relieved after stopping chemotherapy drug pumping, lidocaine arterial pumping through the artery and morphine

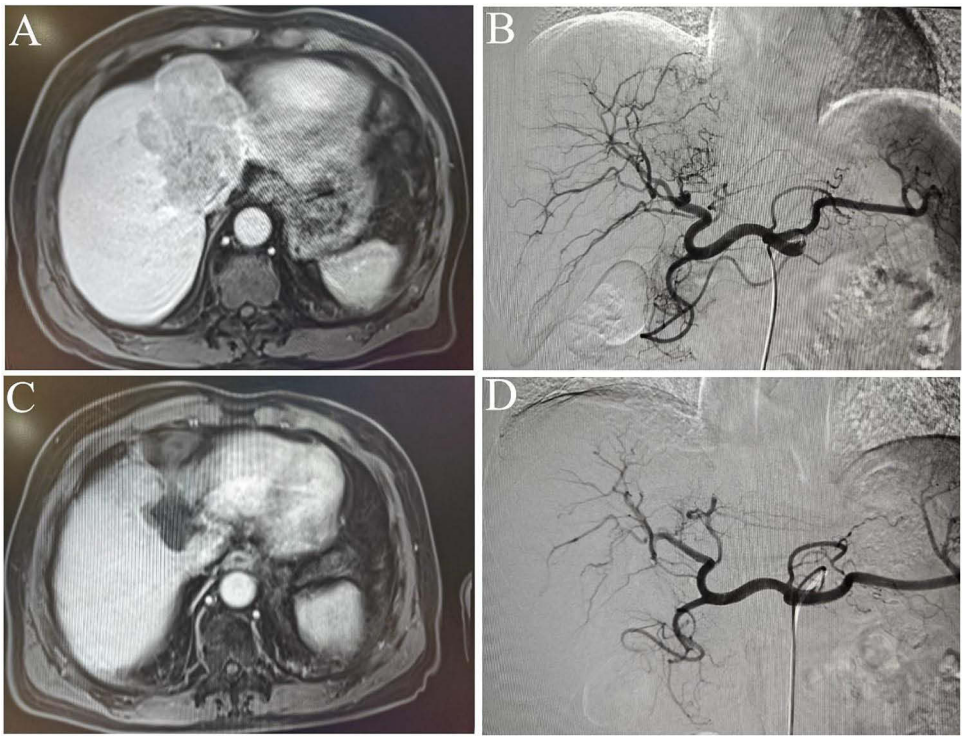


**Figure 2** A 63-year-old male patient with recurrent HCC after hepatectomy was treated with HAIC-apatinib/camrelizumab. (**A**) A contrast-enhanced MR scan showed an 6.8 cm lesion in the liver with significant enhancement. (**B**) Hepatic arteriography showed significant tumor staining. (**C**) After the patient received 3 consecutive combination treatments, MR reexamination showed significant tumor shrinkage without enhancement, which was assessed as complete response according to mRECIST criteria. (**D**) DSA further showed no significant tumor staining.


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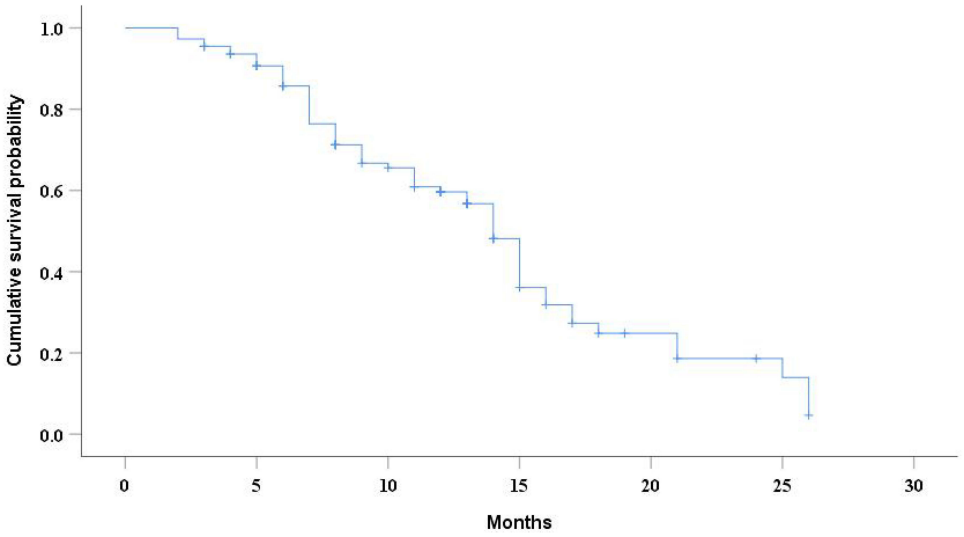


**Figure 3** Kaplan–Meier curve of overall survival in recurrent HCC patients.

analgesic injection. In addition, 90 patients (81.8%) experienced nausea and vomiting of varying degrees at least once during HAIC treatment, and the symptoms were relieved by stopping the pump of chemotherapy drugs, oral administration or intravenous administration of antiemetic drugs. After multiple HAIC, the leukocyte and platelet counts of 20 patients (18.2%)

**Table 2** Univariate Analysis of Prognostic Factors for Overall Survival and Progression-Free Survival

| Variables | OS | | PFS | |
|---|---|---|---|---|
| | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| **Gender** | | | | |
| Male | 1 | | 1 | |
| Female | 0.490 (0.195, 1.227) | 0.128 | 0.775 (0.408, 1.471) | 0.436 |
| **Age (y)** | 1.018 (0.993, 1.043) | 0.166 | 1.012 (0.991, 1.034) | 0.272 |
| **ECOG** | | | | |
| 1 | 1 | | 1 | |
| 0 | 0.800 (0.477, 1.342) | 0.397 | 0.794 (0.504, 1.252) | 0.321 |
| **Hepatitis B** | | | | |
| Yes | 1 | | 1 | |
| No | 0.737 (0.398, 1.364) | 0.331 | 0.671 (0.401, 1.124) | 0.130 |
| **Child-Pugh score** | | | | |
| B | 1 | | 1 | |
| A | 0.826 (0.497, 1.374) | 0.462 | 1.145 (0.729, 1.798) | 0.557 |
| **α-Fetoprotein level** | | | | |
| >400 ng/mL | 1 | | 1 | |
| ≤400 ng/mL | 0.752 (0.451, 1.251) | 0.272 | 0.710 (0.452, 1.114) | 0.136 |
| **Extrahepatic metastases** | | | | |
| Yes | 1 | | 1 | |
| No | 0.746 (0.451, 1.234) | 0.254 | 1.131 (0.730, 1.754) | 0.581 |
| **Largest diameter of tumor (cm)** | 1.053 (0.995, 1.115) | 0.073 | 0.998 (0.948, 1.051) | 0.941 |
| **Tumor number** | | | | |
| ≥3 | 1 | | 1 | |
| <3 | 0.439 (0.211, 0.912) | 0.027 | 0.546 (0.294, 1.012) | 0.055 |

(*Continued*)

**Table 2** (Continued).

| Variables | OS | | PFS | |
|---|---|---|---|---|
| | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| **Vascular invasion** | | | | |
| Present | 1 | | | |
| Absent | 0.546 (0.314, 0.947) | 0.031 | 0.871 (0.552, 1.375) | 0.554 |
| Total bilirubin level (μmol/L) | 0.986 (0.955, 1.017) | 0.364 | 1.003 (0.979, 1.028) | 0.799 |
| Albumin (g/L) | 1.002 (0.956, 1.050) | 0.942 | 1.005 (0.966, 1.045) | 0.811 |
| PT(s) | 0.902 (0.719, 1.131) | 0.371 | 0.872 (0.581, 1.308) | 0.508 |
| AST (μmol/L) | 1.003 (0.999, 1.007) | 0.269 | 0.997 (0.836, 1.189) | 0.971 |
| ALT (μmol/L) | 0.993 (0.984, 1.002) | 0.134 | 0.995 (0.988, 1.003) | 0.212 |
| PLR | 1.003 (1.000, 1.006) | 0.033 | 1.004 (1.001, 1.006) | 0.002 |
| NLR | 1.095(1.009, 1.188) | 0.030 | 1.091 (1.011, 1.178) | 0.025 |

**Abbreviations**: SD, Standard deviation; HR, Hazard ratio; CI, Confidence interval; ECOG, Eastern Cooperative Oncology Group; PT, Prothrombin time; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; PLR, Platelet-to-lymphocyte ratio; NLR, Neutrophil-to-lymphocyte ratio.

**Table 3** Multivariate Analysis of Prognostic Factors for Overall Survival

| Variables | HR (95% CI) | *P* value |
|---|---|---|
| **Largest diameter of tumor (cm)** | 1.022 (0.964, 1.085) | 0.463 |
| **Tumor number** | | |
| ≥3 | 1 | |
| <3 | 0.486 (0.227, 1.040) | 0.063 |
| **Vascular invasion** | | |
| Present | 1 | |
| Absent | 0.564 (0.320, 0.993) | 0.047 |
| PLR | 1.002 (0.998, 1.005) | 0.320 |
| NLR | 1.047 (0.946, 1.158) | 0.375 |

**Abbreviations**: HR, Hazard ratio; CI, Confidence interval; PLR, Platelet-to-lymphocyte ratio; NLR, Neutrophil-to-lymphocyte ratio.

showed progressive decline. In most cases, leukocyte and platelet counts were elevated by infusion of recombinant human granulocyte colony-stimulating factor injection (rhG-CSF) and recombinant human interleukin 11. Meanwhile, partial splenic embolization can increase platelet and white blood cell levels in cirrhotic patients with hypersplenism.

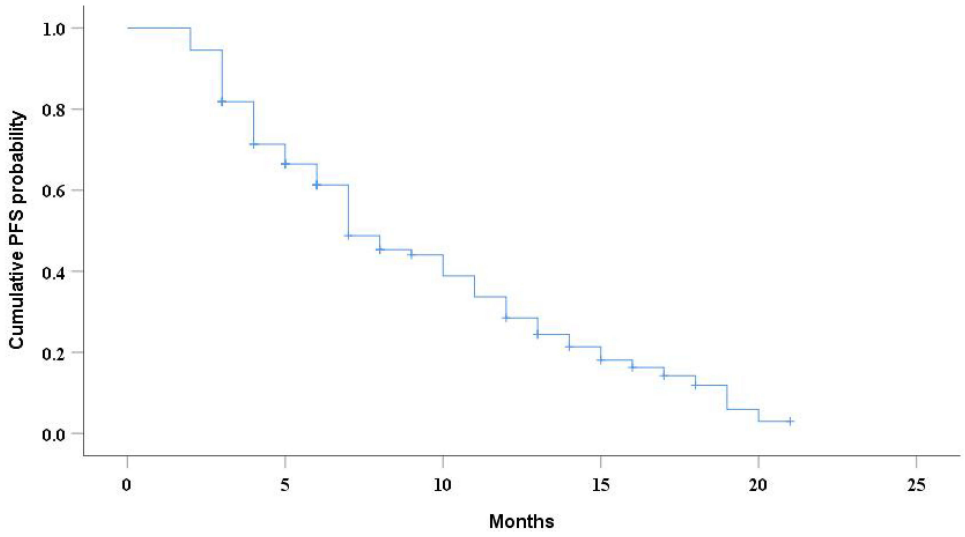


**Figure 4** Kaplan–Meier curve of progression-free survival in recurrent HCC patients.


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**Table 4** Multivariate Analysis of Prognostic Factors for Progression-Free Survival

| Variables | HR (95% CI) | *P* value |
|---|---|---|
| **Tumor number** | | |
| ≥3 | 1 | |
| <3 | 0.588 (0.314, 1.098) | 0.095 |
| **PLR** | 1.003 (1.000, 1.006) | 0.036 |
| **NLR** | 1.020 (0.929, 1.121) | 0.675 |

**Abbreviations**: HR, Hazard ratio; CI, Confidence interval; PLR, Platelet-to-lymphocyte ratio; NLR, Neutrophil-to-lymphocyte ratio.

**Table 5** Adverse Events Related to Apatinib

| Adverse Event | All Events | CTCAE Grade | | |
|---|---|---|---|---|
| | | 1 | 2 | ≥3 |
| Hand-foot skin reactions | 92 (83.6%) | 68 (61.8%) | 24 (21.8%) | 0 (0%) |
| Hypertension | 27 (24.5%) | 18 (16.4%) | 9 (8.2%) | 0 (0%) |
| Bleeding | 1 (0.9%) | 0 (0%) | 0 (0%) | 1 (0.9%) |

**Abbreviation**: CTCAE, Common Terminology Criteria for Adverse Events.

**Table 6** Adverse Events Related to Camrelizumab

| Adverse Event | All Events | CTCAE Grade | | |
|---|---|---|---|---|
| | | 1 | 2 | ≥3 |
| RCCEP | 10 (9.1%) | 5 (4.5%) | 5 (4.5%) | 0 (0%) |
| Hypothyroidism | 5 (4.5%) | 2 (1.8%) | 3 (2.7%) | 0 (0%) |
| Myositis | 1 (0.9%) | 0 (0%) | 1 (0.9%) | 0 (0%) |

**Abbreviations**: ICIs, immune checkpoint inhibitors; CTCAE, Common Terminology Criteria for Adverse Events; RCCEP, Reactive cutaneous capillary endothelial proliferation.

AEs related to apatinib are shown in Table 5. In this study, a total of 120 AEs occurred in 80 patients (72.7%). Hand and foot skin reactions and hypertension are the most common AEs, but they are grade 1–2 and can be improved with symptomatic treatment such as the use of vitamin ointments and taking blood pressure medications. Grade 3 AE occurred in 1 patient, this patient had gingival bleeding and heavy menstruation, and the symptoms were relieved after withdrawal.

AEs related to camrelizumab are shown in Table 6. A total of 16 AEs occurred in 12 patients (10.9%). 10 patients developed reactive cutaneous capillary endothelial proliferation (RCCEP), and 5 patients developed hypothyroidism, but all of them were of grade 1–2. The symptoms were relieved after symptomatic supportive treatment such as thyroxine supplementation. No treatment-related mortalities occurred in this study.

## Discussion

Our preliminary results suggest that HAIC combined with apatinib/camrelizumab is effective and has an acceptable safety profile in recurrent HCC patients after hepatectomy. It is important to note that this study has several important findings that may have implications in clinical practice: (1) For HCC patients with recurrent multiple nodules in the liver who are not suitable for TACE therapy, HAIC combined apatinib/camrelizumab may be a better treatment option; (2) For patients with recurrent HCC, early application of interventional combined target/immunotherapy may well control tumor progression.

The results of this study seem to indicate that HAIC combined with target/immunotherapy is more effective than target/immunotherapy alone for recurrent HCC. In the present study, 61.8% of patients had vascular invasion, 55.5% had extrahepatic metastases, and 49.4% had both, all of which had poor prognosis. However, this study showed an ORR of 31.8%. The ORR of triple therapy for recurrent HCC was significantly better than that of previously reported target/immunotherapy and other first-line therapies (ORR: 2–27.3%).[7,15] Hence, the therapeutic effect of HAIC combined with target/immunotherapy for HCC is better than that of target/immunotherapy or monotherapy, which may be based on the following reasons: (1) The high concentration of chemotherapy drugs in the tumor can directly kill tumor cells, induce immunogenic cell death and enhance the effect of camrelizumab; (2) Apatinib can normalize tumor vessels, increase the penetration of chemotherapy drugs and immune cells, and enhance the efficacy of HAIC and camrelizumab. (3) Camrelizumab enhanced the killing effect of CD8+T cells on tumor cells by blocking PD-1 and PD-L1 pathways.[16–18] Hence, triple therapy can rapidly reduce the tumor burden and improve the therapeutic efficacy of recurrent HCC.

Although TACE has been shown to promote tumor-specific CD8+ T cell responses by killing HCC cells and releasing tumor-associated antigens,[19] it increases tumor hypoxia after incomplete embolization, leading to upregulation of hypoxia-inducible factor-1α, which ultimately leads to increased malignancy of residual tumors.[20,21] Furthermore, repeated TACE treatment can decrease the liver function, and the increase in the number of TACE treatments leads to a decrease in the response rate of tumor tissue to treatment.[22] In this study, the tumor burden was large (mean diameter was 8.5±4.2 cm) and 82.7% of the patients had multiple tumors, which made it difficult to achieve complete embolization. Hence, the application of HAIC combined targeting/immunotherapy in this study is a relatively good choice, and has achieved good efficacy and safety.

Similar to other studies,[23,24] our results indicate that HAIC combined with apatinib/camrelizumab for HCC is safe. After chemotherapy, it is easy to cause bone marrow depression in patients, which is characterized by the decrease of white blood cells and platelets. For patients with significantly reduced platelet counts, splenic artery embolization may be considered. Abdominal pain is another common AEs after HAIC. Previous research has found that oxaliplatin infusion is the main cause, which may be related to oxaliplatin infusion time, hepatic artery diameter, oxaliplatin manufacturer, etc.[25] Prolonged injection time and arterial infusion of lidocaine are effective methods to relieve pain. RCCEP is the common AEs after ICIs treatment. Qin et al indicated that the incidence of RCCEP after camrelizumab treatment was 67%, significantly higher than the incidence of RCCEP in this study.[26] Apatinib can inhibit tumor angiogenesis, so the incidence of RCCEP may be reduced after target/immunotherapy.

This study has certain limitations. Single-center retrospective and non-randomized design are major limitations of this study. Therefore, we intend to conduct a multicenter, prospective study to evaluate HAIC in combination with apatinib/camrelizumab and apatinib/camrelizumab in the treatment of recurrent HCC. Although we identified vascular invasion, PLR, and NLR as prognostic factors, deeper biomarker exploration (including but not limited to ctDNA, IL-6, TNF-α, PD-L1 expression and other inflammatory cytokines) is needed to elucidate the underlying mechanisms of HAIC combined with apatinib and camrelizumab.

## Conclusion

In conclusion, the combination of HAIC and apatinib/camrelizumab has significant efficacy and controllable AEs in patients with recurrent HCC after hepatectomy. Based on the findings of this study, this triple therapy may be a promising treatment option for recurrent HCC patients. Of course, future multicenter prospective studies are needed to validate our observations.

## Data Sharing Statement

All data are available from the corresponding author on reasonable request.

## Acknowledgments

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## Disclosure

The authors have declared that no competing interests exist for this work.

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