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Original Article

Well-established efficacy of camrelizumab combined with radiofrequency ablation in cirrhotic patients with hepatic cancer

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Abstract: Objective: To analyze the efficacy of camrelizumab combined with radiofrequency ablation (RFA) in cirrhotic patients with hepatic cancer. Methods: A total of 89 cirrhotic patients with hepatic cancer were enrolled. The control group (n = 40) received RFA alone, and the research group (n = 49) received camrelizumab combined with RFA. Their clinical data were compared, including efficacy, liver function indicators, inflammatory markers, serum tumor markers, humoral immune function parameters, and incidence of adverse reactions. Factors influencing the efficacy and safety of treatment in these patients were also explored. Results: The research group demonstrated a significantly higher total effective rate than the control group (89.80% vs. 70.00%, P = 0.018). Post-treatment, the research group had significantly lower liver function indicators (serum total bilirubin (TBIL), alanine aminotransferase (ALT), aspartate aminotransferase (AST)), inflammatory markers (Interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), high-sensitivity c-reactive protein (hs-CRP)), and serum tumor markers (alpha-fetoprotein (AFP), liver cancer paternally expressed gene 10 (PEG10), and carbohydrate antigen 199 (CA199)) (all P<0.05). In contrast, the research group had significantly higher humoral immune function parameters (immunoglobulin A (IgA), IgG, IgM), with statistically significant differences (all P<0.05). There was no significant difference in the incidence of adverse reactions between the two groups (P = 0.864). Finally, Child-Pugh Class B, tumor size ≥4 cm, AST ≥77 U/L, AFP ≥420 μg/L, and treatment with RFA alone were found to be associated with an increased risk of treatment failure or adverse events (all P<0.05). Conclusion: The combination of camrelizumab and RFA demonstrates superior efficacy in the treatment of cirrhotic patients with hepatic cancer.

Keywords: Camrelizumab, radiofrequency ablation, hepatic cirrhosis, hepatic cancer, efficacy, liver function

Introduction

Hepatic cancer, a major global health burden, ranks as the fourth leading cause of cancer-related mortality worldwide [1]. Its etiology involves chronic hepatitis B (CHB) virus infection and other potential factors (e.g., non-alcoholic steatohepatitis, heavy alcohol consumption) [2]. CHB induces immune disorders through multiple pathways, leading to persistent liver dysfunction, cirrhosis (a precursor to hepatic cancer), and ultimately hepatic cancer [3]. The pathological mechanism in cirrhotic patients with hepatic cancer is complex, possibly associated with processes such as hepatic stellate cell activation, sinusoidal capillarization, and renin-angiotensin-aldosterone system dysregulation, which pose significant therapeutic challenges [4]. Currently, various treatment approaches are available for hepatic cancer patients, including non-curative therapies (e.g., intra-arterial therapy, radiotherapy, systemic therapy) and curative therapies (e.g., surgical resection, liver transplantation, radiofrequency ablation (RFA)) [5]. However, few studies have explored the therapeutic effects in cirrhotic

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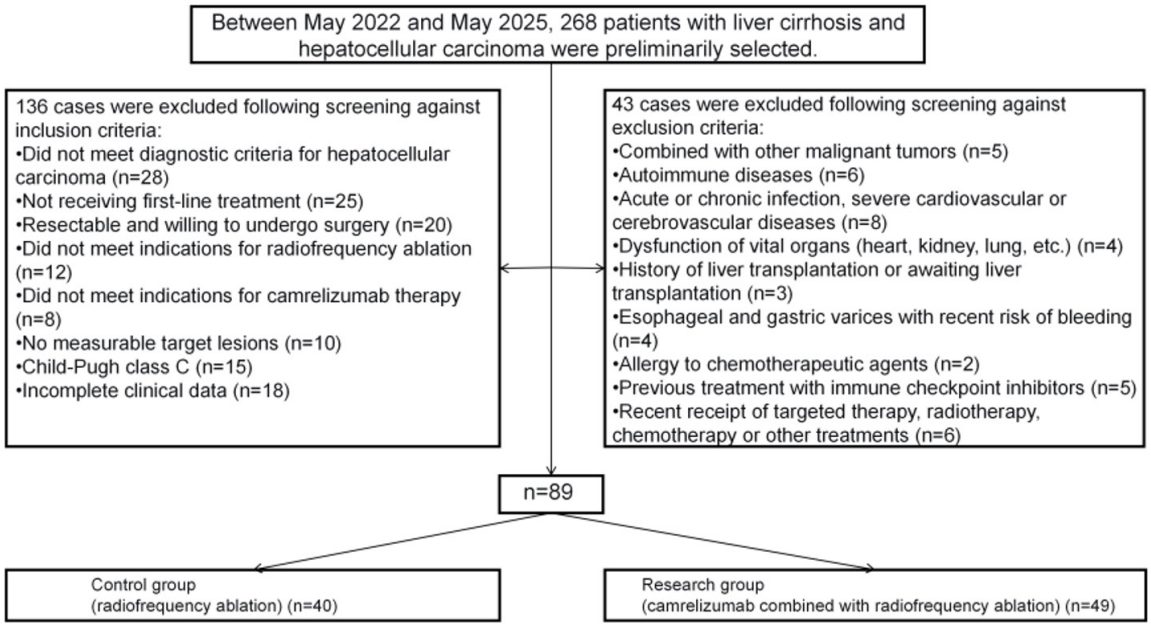

Figure 1. Patient screening flowchart.

patients with hepatic cancer. To further improve efficacy in this patient population, we conducted relevant analyses and validation studies.

This study compared the clinical outcomes of RFA alone versus camrelizumab combined with RFA in the treatment of cirrhotic patients with hepatic cancer. RFA is a percutaneous thermal ablation technique that yields prognostic outcomes (overall survival) comparable to those of microwave ablation in patients with hepatocellular carcinoma (HCC) [6]. Compared with surgical resection, RFA is associated with lower postoperative complication rates and shorter procedure durations in cirrhotic patients with hepatic cancer; however, its 1- to 3-year prognostic outcomes are inferior to those of surgical resection [7]. Camrelizumab is a humanized monoclonal antibody targeting programmed cell death protein-1 (PD-1), which exhibits high antitumor activity and favorable tolerability across multiple solid tumors [8]. It serves as a first-line therapy for inoperable HCC patients, and its combination with apatinib as a hepatic artery infusion chemotherapy intervention has shown promising efficacy and safety profiles in HCC patients [9]. Few studies have investigated the effects of camrelizumab combined with RFA on efficacy, liver function, and serum tumor markers in cirrhotic patients with hepatic cancer. Therefore, we conducted relevant analyses to optimize clinical management for this patient population.

The innovation of this study lies in its multidimensional validation of the clinical benefits of camrelizumab combined with RFA in cirrhotic patients with hepatic cancer, evaluated through efficacy, liver function, inflammatory markers, serum tumor markers, humoral immune function, and incidence of adverse reactions. Additionally, the study innovatively introduced a composite endpoint integrating efficacy and safety, systematically identified key factors influencing patients' achievement of optimal treatment outcomes, and provided multidimensional, evidence-based support for personalized treatment decisions in this population.

Materials and methods

Patient screening

Eighty-nine cirrhotic patients with hepatic cancer admitted to Renmin Hospital of Wuhan University from May 2022 to May 2025 were selected as study subjects. They were grouped based on the actual treatment regimen received: 40 in the control group (receiving RFA alone) and 49 in the research group (receiving camrelizumab combined with RFA). This study was approved by the Ethics Committee of Renmin Hospital of Wuhan University. The patient screening process is shown in **Figure 1**.

Inclusion criteria: Diagnosed with hepatic cancer based on clinical presentation, laboratory

findings, and imaging examinations [10]; meeting the diagnostic criteria for hepatic cirrhosis [11]; treatment-naive; with unresectable disease or unwillingness to undergo surgery; eligible for RFA and camrelizumab therapy; presence of measurable target lesions; Child-Pugh classification of grades A-B [12]; and complete clinical data.

Exclusion criteria: Concurrent malignant tumors; presence of inflammatory bowel disease, systemic lupus erythematosus, or rheumatoid arthritis; acute or chronic infections; serious cardiovascular or cerebrovascular diseases; dysfunction of vital organs (e.g., heart, kidney, lung); history of liver transplantation or awaiting liver transplantation; esophageal or gastric varices at risk of recent bleeding; allergy to chemotherapy drugs; history of treatment with immune checkpoint inhibitors; recent receipt of targeted therapy, radiotherapy, chemotherapy, or other treatments; life expectancy of less than 3 months; pregnant or lactating patients; and autoimmune diseases or coagulation disorders.

Treatment methods

The control group underwent RFA. For tumors >4.0 cm in diameter, repeated ablation procedures were performed to enhance efficacy. Needle insertion sites were selected near the original ablation points, with ablation extending at least 0.5 cm beyond the tumor margins. Postoperatively, patients received hepatoprotective and anti-inflammatory therapy, and their vital signs and postoperative complications were closely monitored.

The research group received camrelizumab in addition to the regimen adopted in the control group. Two weeks prior to treatment, patients received camrelizumab (200 mg/vial) at 3 mg/kg intravenously. A second intravenous dose was administered one week postoperatively, followed by subsequent intravenous infusions every three weeks until disease progression or intolerable drug toxicity. All patients were treated for two months.

The treatment regimens in this study were not selected randomly; instead, they were individually determined by physicians following a comprehensive assessment of each patient's condition, financial situation, and treatment preferences. All patients were fully informed of the benefits and risks associated with the different treatment options.

Clinical data extraction

Clinical data were collected via the hospital's electronic medical record system, including: 1) General data: age, gender, duration of cirrhosis, history of hypertension, history of diabetes, history of alcohol consumption, family history of hepatic cancer, Child-Pugh classification, tumor size, number of tumors, and Barcelona Clinic Liver Cancer (BCLC) staging; 2) Treatment efficacy; 3) Liver function: Total bilirubin (TBIL), alanine Aminotransferase (ALT), aspartate aminotransferase (AST); 4) Inflammatory markers: Interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), high-sensitivity C-reactive protein (hs-CRP); 5) Serum tumor markers: alpha-fetoprotein (AFP), liver cancer paternally expressed gene 10 (PEG10), carbohydrate antigen 199 (CA199); 6) Humoral immune function: immunoglobulin A (IgA), IgG, IgM; 7) Adverse reactions: occurrence of adverse events during treatment, including fever, haematochezia, rash, shock, and thyroid dysfunction.

Outcome measures

Efficacy [13]. Efficacy assessment of liver cancer lesions was conducted 2 months after treatment by integrating the modified Response Evaluation Criteria in Solid Tumors, patient liver function indicators, and abdominal Computed Tomography (CT) findings. Markedly effective was defined as CT showing complete disappearance of tumor lesions, restoration of liver function to the normal range, and complete resolution of clinical symptoms. Effective was defined as CT showing complete disappearance of tumor lesions, significant improvement in liver function compared to pre-treatment, and substantial relief of clinical symptoms. Ineffective was defined as CT showing new tumor lesions within the liver, no significant improvement in liver function, and no notable change in clinical symptoms. The total effective rate was calculated as the percentage of patients with markedly effective or effective outcomes relative to the total number of patients.

Liver function. Before treatment and 2 months after treatment, 5 mL of peripheral venous blood was drawn from patients in both groups on an empty stomach in the morning. After centrifugation, serum was obtained and analyzed using a fully automated biochemical analyzer to measure TBIL, ALT, and AST levels.

Inflammatory markers. IL-6, TNF-α, and hs-CRP levels in serum were measured using enzyme-linked immunosorbent assay (ELISA) before treatment and 7 days after treatment.

Serum tumor markers. Serum levels of AFP, PEG10, and CA199 were measured using ELISA before treatment and 2 months after treatment.

Humoral immune function. ELISA was applied to measure the levels of IgA, IgG, and IgM in patient serum before treatment and 2 months after treatment.

Adverse reactions: The number of adverse events (including fever, haematochezia, rash, shock, and thyroid dysfunction) occurring in all patients during the treatment period was monitored and documented, and the incidence was calculated.

Among the above parameters, treatment efficacy, liver function, serum tumor markers, and adverse reactions are primary endpoints, while inflammatory markers and humoral immune function are secondary endpoints.

Statistical analysis

Measurement data were statistically described as mean ± standard deviation (SD), with comparisons between the two groups using the independent sample t-test and comparisons before and after treatment within the same group using the paired t-test. Enumeration data were presented as percentages (%), with comparisons between the two groups using the chi-square test. Factors influencing efficacy and safety were assessed by univariate and binary logistic regression analysis. Variables with a *p*-value <0.05 in the univariate analysis were included in the multivariate analysis, which was conducted using the Enter method. SPSS 22.0 statistical software was used for data analysis. A *P* value <0.05 was considered statistically significant. Sample sizes were calculated using PASS 15.0 software. Assuming an effective rate of 60% in the control group and 84% in the research group, with $\alpha = 0.05$ (two-sided test) and $\beta = 0.20$ (power 80%), the estimated sample size was at least 45 cases per group, totaling 90 subjects. This study ultimately enrolled 89 subjects, which basically met the sample size requirements for primary efficacy comparison.

Results

General data

Table 1 presents no significant differences between the control and the research groups in terms of age, gender, duration of hepatic cirrhosis, history of hypertension, history of diabetes, history of alcohol consumption, family history of hepatic cancer, Child-Pugh classification, tumor size, number of tumors, or BCLC staging (all P>0.05).

Efficacy

As shown in **Table 2**, the total effective rate was 70.00% in the control group, which was significantly lower than the 89.80% in the research group (P = 0.018).

Liver function

Table 3 presents the results of liver function indicators. No significant differences were observed in pre-treatment TBIL, ALT, and AST levels between the two groups (all P>0.05). After treatment, all these indicators decreased to varying degrees, with lower values in the research group (all P<0.05).

Inflammatory markers

As presented in **Table 4**, no significant differences were found in pre-treatment inflammatory markers (IL-6, TNF-α, hs-CRP) between the two groups (all P>0.05). After treatment, all these indicators decreased significantly (all P<0.001), with lower values in the research group (all P<0.05).

Serum tumor markers

As illustrated in **Figure 2**, there were no significant differences in pre-treatment levels of AFP, PEG10, and CA199 between the two groups (all P>0.05). After treatment, all these indicators

Table 1. General data

Data	Control group (n = 40)	Research group (n = 49)	χ^2/t/Z	P
Age (years)	51.70 ± 7.30	51.29 ± 7.26	0.264	0.792
Gender			0.431	0.512
Male	24 (60.00)	26 (53.06)		
Female	16 (40.00)	23 (46.94)		
Duration of hepatic cirrhosis (years)	7.00 (5.25, 7.00)	6.00 (5.00, 8.00)	-0.100	0.920
History of hypertension			0.083	0.774
Absent	20 (50.00)	26 (53.06)		
Present	20 (50.00)	23 (46.94)		
History of diabetes			0.072	0.789
Absent	28 (70.00)	33 (67.35)		
Present	12 (30.00)	16 (32.65)		
History of alcohol consumption			1.287	0.257
Absent	16 (40.00)	14 (28.57)		
Present	24 (60.00)	35 (71.43)		
Family history of hepatic cancer			0.267	0.606
Absent	30 (75.00)	39 (79.59)		
Present	10 (25.00)	10 (20.41)		
Child-Pugh classification			0.496	0.481
Grade A	15 (37.50)	22 (44.90)		
Grade B	25 (62.50)	27 (55.10)		
Tumor size (cm)			0.041	0.839
<6	18 (45.00)	21 (42.86)		
≥6	22 (55.00)	28 (57.14)		
Number of tumors			0.351	0.553
<2	22 (55.00)	30 (61.22)		
≥2	18 (45.00)	19 (38.78)		
BCLC staging			0.083	0.774
0+A	20 (50.00)	26 (53.06)		
B+C+D	20 (50.00)	23 (46.94)		

Note: BCLC, Barcelona Clinic Liver Cancer.

Table 2. Efficacy

Efficacy	Control group (n = 40)	Research group (n = 49)	χ^2	P
Markedly effective	13 (32.50)	20 (40.82)		
Effective	15 (37.50)	24 (48.98)		
Ineffective	12 (30.00)	5 (10.20)		
Total effective rate	28 (70.00)	44 (89.80)	5.585	0.018

decreased significantly (all P<0.05), and were lower in the research group (all P<0.05).

Humoral immune function

Figure 3 shows no significant difference in the levels of IgA, IgG, and IgM between the two groups before treatment (all P>0.05). After treatment, all these humoral immune function parameters increased significantly (all P<0.05), and were higher in the research group (all P<0.05).

Incidence of adverse reactions

As shown in **Table 5**, the control group had 2 cases of fever, 2 cases of haematochezia, 1 case of rash, 1 case of shock, and 0 cases of thyroid dysfunction. The research group had 2 cases of fever, 2 cases of haematochezia, 1 case of rash, 0 cases of shock, and 3 cases of thyroid dysfunction. The overall incidence of adverse reactions was 15.00% in the control group and 16.33% in the research group, with no significant difference (P>0.05).

Table 3. Liver function

Indicator	Control group (n = 40)	Research group (n = 49)	t	P
TBIL (mmol/L)				
Before treatment	37.10 ± 7.97	37.55 ± 7.83	0.268	0.790
After treatment	34.40 ± 6.64***	29.29 ± 6.70***	3.594	<0.001
t	1.646	5.611		
P	0.104	<0.001		
ALT (U/L)				
Before treatment	62.17 ± 11.91	61.57 ± 10.22	0.256	0.799
After treatment	51.23 ± 10.88***	46.24 ± 9.23***	2.341	0.022
t	4.289	7.792		
P	<0.001	<0.001		
AST (U/L)				
Before treatment	76.92 ± 13.16	77.31 ± 12.13	0.145	0.885
After treatment	71.12 ± 9.40***	65.90 ± 7.82***	2.860	0.005
t	2.826	5.534		
P	0.006	<0.001		

Note: TBIL, total bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase. ***P < 0.001, intragroup comparison with pre-treatment results.

Table 4. Inflammatory markers

Marker	Control group (n = 40)	Research group (n = 49)	t	P
IL-6 (pg/mL)				
Before treatment	71.65 ± 9.02	74.37 ± 8.78	1.436	0.155
After treatment	150.30 ± 20.09***	125.51 ± 14.38***	6.773	<0.001
t	22.588	21.247		
P	<0.001	<0.001		
TNF-α (pg/mL)				
Before treatment	8.22 ± 2.71	9.02 ± 3.23	1.248	0.215
After treatment	25.62 ± 5.29***	19.06 ± 4.96***	6.024	<0.001
t	18.515	11.874		
P	<0.001	<0.001		
hs-CRP (mg/L)				
Before treatment	2.37 ± 0.97	2.28 ± 0.84	0.469	0.640
After treatment	9.84 ± 4.24***	8.06 ± 2.47***	2.471	0.015
t	10.862	15.508		
P	<0.001	<0.001		

Note: IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; hs-CRP, high-sensitivity C-reactive protein. ***P < 0.001, intragroup comparison with pre-treatment results.

Factors influencing efficacy and safety in cirrhotic patients with hepatic cancer

Patients were divided into two groups based on efficacy and safety outcomes: the ideal responder group (n = 63) and the non-ideal responder group (n = 26). The former included patients who responded effectively to treatment and experienced no safety concerns, while the latter included patients who did not respond to treatment and/or experienced adverse reactions. Univariate analysis (**Table 6**) revealed no significant differences between the two groups in terms of age, gender, duration of hepatic cirrhosis, history of hypertension, history of diabetes, history of alcohol consumption, family history of hepatic cancer, number of tumors, pre-treatment TBIL, pre-treatment ALT, pre-treatment IL-6, pre-treatment TNF-α, pre-treatment PEG10, pre-treatment CA199, and pre-treatment IgA/G/M levels (all P>0.05). In contrast, Child-Pugh classification, tumor size,

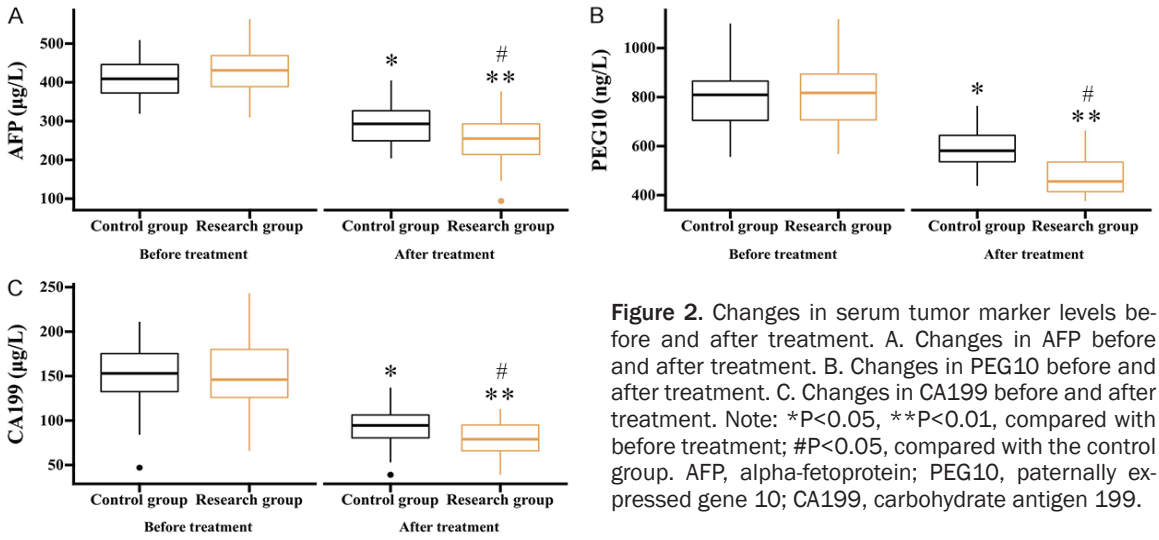

Figure 2. Changes in serum tumor marker levels before and after treatment. A. Changes in AFP before and after treatment. B. Changes in PEG10 before and after treatment. C. Changes in CA199 before and after treatment. Note: *P<0.05, **P<0.01, compared with before treatment; #P<0.05, compared with the control group. AFP, alpha-fetoprotein; PEG10, paternally expressed gene 10; CA199, carbohydrate antigen 199.

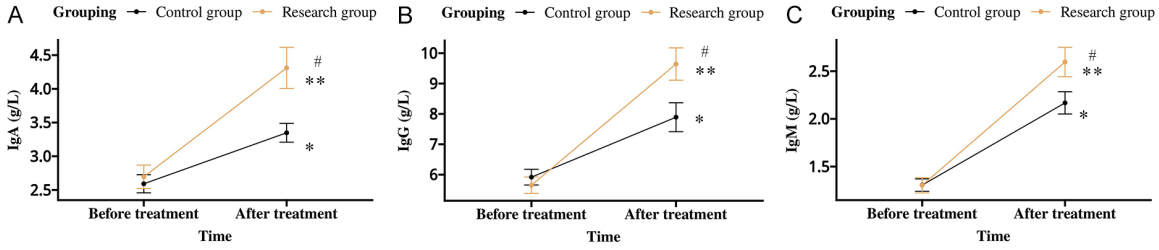

Figure 3. Changes in humoral immune function parameter levels before and after treatment. A. Changes in IgA before and after treatment. B. Changes in IgG before and after treatment. C. Changes in IgM before and after treatment. Note: *P<0.05, **P<0.01, compared with before treatment; #P<0.05, compared with the control group. Ig, immunoglobulin.

Table 5. Incidence of adverse reactions

Adverse event	Control group (n = 40)	Research group (n = 49)	χ^2	P
Fever	2 (5.00)	2 (4.08)		
Haematochezia	2 (5.00)	2 (4.08)		
Rash	1 (2.50)	1 (2.04)		
Shock	1 (2.50)	0 (0.00)		
Thyroid dysfunction	0 (0.00)	3 (6.12)		
Total	6 (15.00)	8 (16.33)	0.029	0.864

BCLC staging, pre-treatment AST, pre-treatment hs-CRP, pre-treatment AFP, and treatment method were closely associated with efficacy and safety in cirrhotic patients with hepatic cancer (all P<0.05). These factors with significant differences were included as independent variables in multivariate analysis (**Table 7**), with continuous variables divided at the median. Multivariate analysis (**Table 8**) demonstrated that Child-Pugh classification, tumor size, pre-treatment AST, and pre-treatment AFP were all risk factors for efficacy and safety in cirrhotic patients with hepatic cancer (all P<0.05), while treatment method was a protective factor (P = 0.010). In addition, BCLC staging and pre-treatment hs-CRP were not factors influencing efficacy and safety in this patient population (both P>0.05).

Discussion

RFA is minimally invasive, safe, easy to operate, and cost-effective, making it the preferred local ablation therapy for hepatic cancer patients. However, it has a longer response time and exhibits individual heterogeneity [14]. Based on the premise that tumor immunotherapy combined with RFA further enhances clinical benefits for cirrhotic patients with hepatic cancer, this study was

Table 6. Univariate analysis of factors influencing the efficacy and safety in cirrhotic patients with hepatic cancer

Item	Ideal responder group (n = 63)	Non-ideal responder group (n = 26)	χ^2	P
Age (years)			0.351	0.553
<52 (n = 42)	31 (49.21)	11 (42.31)		
≥52 (n = 47)	32 (50.79)	15 (57.69)		
Gender			0.570	0.450
Male (n = 50)	37 (58.73)	13 (50.00)		
Female (n = 39)	26 (41.27)	13 (50.00)		
Duration of hepatic cirrhosis (years)			2.151	0.142
<7 (n = 45)	35 (55.56)	10 (38.46)		
≥7 (n = 44)	28 (44.44)	16 (61.54)		
History of hypertension			0.069	0.793
Absent (n = 46)	32 (50.79)	14 (53.85)		
Present (n = 43)	31 (49.21)	12 (46.15)		
History of diabetes			0.835	0.361
Absent (n = 61)	45 (71.43)	16 (61.54)		
Present (n = 28)	18 (28.57)	10 (38.46)		
History of alcohol consumption			2.546	0.111
Absent (n = 30)	18 (28.57)	12 (46.15)		
Present (n = 59)	45 (71.43)	14 (53.85)		
Family history of hepatic cancer			3.109	0.078
Absent (n = 69)	52 (82.54)	17 (65.38)		
Present (n = 20)	11 (17.46)	9 (34.62)		
Child-Pugh classification			5.173	0.023
Grade A (n = 37)	31 (49.21)	6 (23.08)		
Grade B (n = 52)	32 (50.79)	20 (76.92)		
Tumor size (cm)			4.260	0.039
<6 (n = 39)	32 (50.79)	7 (26.92)		
≥6 (n = 50)	31 (49.21)	19 (73.08)		
Number of tumors			0.317	0.573
<2 (n = 52)	38 (60.32)	14 (53.85)		
≥2 (n = 37)	25 (39.68)	12 (46.15)		
BCLC staging			6.435	0.011
0+A (n = 46)	38 (60.32)	8 (30.77)		
B+C+D (n = 43)	25 (39.68)	18 (69.23)		
Pre-treatment TBIL (mmol/L)			0.229	0.633
<37 (n = 41)	28 (44.44)	13 (50.00)		
≥37 (n = 48)	35 (55.56)	13 (50.00)		
Pre-treatment ALT (U/L)			0.286	0.593
<62 (n = 44)	30 (47.62)	14 (53.85)		
≥62 (n = 45)	33 (52.38)	12 (46.15)		
Pre-treatment AST (U/L)			5.779	0.016
<77 (n = 38)	32 (50.79)	6 (23.08)		
≥77 (n = 51)	31 (49.21)	20 (76.92)		
Pre-treatment IL-6 (pg/mL)			0.022	0.883
<75 (n = 49)	35 (55.56)	14 (53.85)		
≥75 (n = 40)	28 (44.44)	12 (46.15)		

Pre-treatment TNF-α (pg/mL)			0.159	0.691
<9 (n = 44)	32 (50.79)	12 (46.15)		
≥9 (n = 45)	31 (49.21)	14 (53.85)		
Pre-treatment hs-CRP (mg/L)			6.202	0.013
<2.50 (n = 49)	40 (63.49)	9 (34.62)		
≥2.50 (n = 40)	23 (36.51)	17 (65.38)		
Pre-treatment AFP (μg/L)			8.570	0.003
<420 (n = 42)	36 (57.14)	6 (23.08)		
≥420 (n = 47)	27 (42.86)	20 (76.92)		
Pre-treatment PEG10 (ng/L)			0.209	0.648
<800 (n = 41)	30 (47.62)	11 (42.31)		
≥800 (n = 48)	33 (52.38)	15 (57.69)		
Pre-treatment CA199 (μg/L)			0.531	0.466
<150 (n = 43)	32 (50.79)	11 (42.31)		
≥150 (n = 46)	31 (49.21)	15 (57.69)		
Pre-treatment IgA (g/L)			0.016	0.900
<2.70 (n = 47)	33 (52.38)	14 (53.85)		
≥2.70 (n = 42)	30 (47.62)	12 (46.15)		
Pre-treatment IgG (g/L)			0.570	0.450
<6.00 (n = 50)	37 (58.73)	13 (50.00)		
≥6.00 (n = 39)	26 (41.27)	13 (50.00)		
Pre-treatment IgM (g/L)			0.022	0.883
<1.30 (n = 40)	28 (44.44)	12 (46.15)		
≥1.30 (n = 49)	35 (55.56)	14 (53.85)		
Treatment method			4.088	0.043
Radiofrequency ablation (n = 40)	24 (38.10)	16 (61.54)		
Camrelizumab plus radiofrequency ablation (n = 49)	39 (61.90)	10 (38.46)		

Note: BCLC, Barcelona Clinic Liver Cancer; TBIL, total bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; hs-CRP, high-sensitivity C-reactive protein; AFP, alpha-fetoprotein; PEG10, paternally expressed gene 10; CA199, carbohydrate antigen 199; Ig, immunoglobulin.

conducted to analyze, verify, and report these outcomes.

This study first revealed that camrelizumab combined with RFA increased the effective rate from 70.00% to 89.80% in cirrhotic patients with hepatic cancer, demonstrating that this combination effectively achieves lesion control, restores liver function, and alleviates clinical symptoms. RFA promotes tumor antigen-specific T-cell responses, which enhance the effects of immunotherapy within the tumor microenvironment, thereby synergistically improving efficacy in cirrhotic patients with hepatic cancer [15]. Moreover, studies have indicated that preparing lenvatinib-loaded vesicles using PD-1-overexpressing macrophage membranes enhances the efficacy of immunotherapy against HCC recurrence following RFA; tumor recurrence after ablation is prevented by leveraging potent T-cell anti-tumor memory effects [16]. The results of liver function indicators (TBIL, ALT, AST) showed that liver function in cirrhotic patients with hepatic cancer was effectively restored under the combined therapy intervention. The mechanism may lie in the synergistic immune activation effect produced by RFA combined with anti-PD-1 therapy. Although RFA induces tumor-specific T-cell responses, it also upregulates PD-L1, leading to immune suppression. However, the addition of PD-1 inhibitors can reverse this suppression, enhance and sustain antitumor immunity, and thereby potentially mitigate liver injury [17].

Regarding the inflammatory markers IL-6, TNF-α, and hs-CRP, the combination therapy exerted a more pronounced anti-inflammatory effect in cirrhotic patients with hepatic cancer, effectively reducing inflammation 7 days postopera-

Table 7. Assignment table

Item	Definition	Variable	Coding
Child-Pugh classification	Liver function classification	X1	Grade A = 0, grade B = 1
Tumor size (cm)	Maximum tumor diameter	X2	<6 = 0, ≥6 = 1
BCLC staging	Clinical stage of liver cancer	X3	0+A = 0, B+C+D = 1
Pre-treatment AST (U/L)	Liver function indicator	X4	<77 = 0, ≥77 = 1
Pre-treatment hs-CRP (mg/L)	Inflammatory marker	X5	<2.50 = 0, ≥2.50 = 1
Pre-treatment AFP (μg/L)	Serum tumor marker	X6	<420 = 0, ≥420 = 1
Treatment method	Basis for study grouping	X7	RFA = 0, camrelizumab combined with RFA = 1
Efficacy and safety	Composite outcome	Y	Ideal responder (who responded effectively to treatment and experienced no adverse reactions) = 0, non-ideal responder (who did not respond to treatment and/or experienced adverse reactions) = 1

Note: BCLC, Barcelona Clinic Liver Cancer; AST, aspartate aminotransferase; hs-CRP, high-sensitivity C-reactive protein; AFP, alpha-fetoprotein; RFA, radiofrequency ablation.

Table 8. Multivariate analysis of factors influencing efficacy and safety in cirrhotic patients with hepatic cancer

Item	B	SE	WALD	P	OR	95% CI
Child-Pugh classification	1.432	0.728	3.872	0.049	4.185	1.006-17.417
Tumor size (cm)	1.808	0.703	6.614	0.010	6.098	1.537-24.185
BCLC staging	0.907	0.656	1.914	0.166	2.477	0.685-8.955
Pre-treatment AST (U/L)	1.809	0.695	6.769	0.009	6.103	1.562-23.842
Pre-treatment hs-CRP (mg/L)	0.947	0.626	2.290	0.130	2.577	0.756-8.784
Pre-treatment AFP (μg/L)	1.877	0.727	6.673	0.010	6.534	1.573-27.143
Treatment method	-1.485	0.674	4.848	0.028	0.227	0.060-0.849

Note: SE, standard error; OR, odds ratio; 95% CI, 95% confidence interval; BCLC, Barcelona Clinic Liver Cancer; AST, aspartate aminotransferase; hs-CRP, high-sensitivity C-reactive protein; AFP, alpha-fetoprotein.

tively. The imbalance in the inflammatory microenvironment of cirrhotic patients with hepatic cancer may be closely associated with hepatic systemic factors (e.g., lipid overload, lipotoxicity, oxidative stress) and extrahepatic factors (e.g., the gut-liver axis), which may further exacerbate liver injury and fibrosis [18, 19]. The inhibitory effect of the combination therapy on inflammation in cirrhotic patients with hepatic cancer may be related to the ability of camrelizumab to eliminate residual lesions associated with RFA, thereby helping to suppress the release of pro-inflammatory cytokines [20]. Camrelizumab combined with RFA significantly suppressed serum tumor markers (AFP, PEG10, CA199) in cirrhotic patients with hepatic cancer. In a mouse subcutaneous tumor study by Tian et al. [21], more potent antitumor immune responses were observed when RFA was combined with the immunomodulator Resiquimod. This approach effectively suppressed hepatic cancer progression via a natural killer (NK)-cell-dependent mechanism, inhibited tumor angiogenesis, and promoted tumor cell apoptosis. These findings partially explain the mechanism underlying the effective reduction in serum tumor marker levels observed with the combination therapy in this study.

Based on the results of humoral immune function (IgA, IgG, IgM), the combined therapy significantly enhanced systemic humoral immune function in cirrhotic patients with hepatic cancer. This may be attributed to the combined therapy's ability to inhibit disease progression, improve liver function, and reduce inflammation in patients. Regarding safety, no significant increase in the overall incidence of adverse reactions was observed in cirrhotic patients with hepatic cancer following the application of the combined therapy, demonstrating favorable tolerability. Finally, through univariate and multivariate analyses, Child-Pugh grade B, tumor size ≥4 cm, pre-treatment AST ≥77 U/L, pre-treatment AFP ≥420 μg/L, and treatment

with RFA alone were identified as factors increasing the risk of treatment failure or adverse reactions in cirrhotic patients with hepatic cancer.

This study has several limitations. First, the sample size was only 89 patients, all from a single region, which may limit the representativeness of the sample. Second, in-depth investigations into the potential mechanisms of action of camrelizumab were not conducted. Third, the follow-up period was short, and long-term survival outcomes (e.g., progression-free survival, overall survival) and long-term adverse reactions were not tracked and evaluated. Finally, the sample size in this study was relatively small for multivariate logistic regression analysis, so the results of the factor analysis may be subject to overfitting and instability, and should be interpreted as exploratory findings.

Therefore, future studies should include a broader sample from different regions to enhance the generalizability of the findings. In addition, in vitro and in vivo studies should be performed to further explore the underlying mechanisms of action of camrelizumab. Meanwhile, the follow-up period needs to be extended to clarify the long-term benefits and risks of the combination regimen. Finally, further verification with a larger sample size is required to confirm the reliability of the factors influencing treatment efficacy and safety.

In summary, in cirrhotic patients with hepatic cancer, camrelizumab combined with RFA significantly enhances treatment efficacy, alleviates clinical symptoms, improves liver function and humoral immunity, suppresses inflammatory and serum tumor markers, while maintaining clinical safety. Moreover, cirrhotic patients with hepatic cancer presenting with clinical characteristics such as Child-Pugh grade B, tumor size ≥4 cm, pre-treatment AST ≥77 U/L, pre-treatment AFP ≥420 μg/L, and treatment with RFA alone have a significantly increased risk of treatment failure or adverse reactions.

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Disclosure of conflict of interest

None.

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