Comparison of the Efficacy of Transcatheter Arterial Chemoembolization Combined with Radiofrequency Ablation Versus Monotherapy in Patients with Liver Cancer

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AIM: This study assesses the effectiveness of combining transcatheter arterial chemoembolization (TACE) and radiofrequency ablation (RFA) in treating hepatocellular carcinoma (HCC).

METHODS: Retrospective analysis of 125 HCC patients treated from 2020 to 2021, divided into two groups: monotherapy using TACE (n = 63), and a combined approach of RFA and TACE (n = 62). Comparison factors included clinical efficacy, liver function, tumor markers, complications, quality of life, and prognosis.

RESULTS: The combined treatment group showed higher effectiveness ($p < 0.05$), improved liver function and tumor marker levels 4 weeks post-treatment ($p < 0.05$), significantly fewer complications ($p < 0.05$), and enhanced quality of life at the year-long follow-up ($p < 0.05$). The prognosis was better in the combination group, demonstrated by fewer recurrences and higher 1-year survival rates ($p < 0.05$).

CONCLUSIONS: The dual approach of TACE and RFA shows improved results for HCC patients, including improved liver function, reduced tumor markers, fewer complications, and superior quality of life and prognosis. Consequently, combined treatment approach is endorsed for clinical practice.

Keywords: transcatheter arterial chemoembolization; radiofrequency ablation; hepatocellular carcinoma; complications; quality of life

Introduction

Liver cancer, particularly hepatocellular carcinoma (HCC), is the 3rd leading cause of cancer-related death worldwide and one of the leading causes of death in patients with cirrhosis [1]. In fact, nearly 90% of liver cancer diagnoses were identified as HCC [2]. The preferred treatment mode is mainly therapeutic surgery; however, the early stages of liver cancer are often disguised by uncharacteristic symptoms and stealthy progression. Additional complications including multiple nodules, multicentric lesions, and comorbid conditions such as liver cirrhosis and portal hypertension, further interfere with medical imaging examinations. Consequently, optimal opportunities for surgical intervention may be overlooked [3].

Among patients with advanced HCC, who for various reasons may not be eligible for surgery, clinical approaches mainly advocate treatments like transcatheter arterial chemoembolization (TACE), radiofrequency ablation (RFA), along with molecular targeted therapy, and radiation therapy [4]. TACE, an interventional technique often employed in clinical scenarios, continues to demonstrate suboptimal efficacy [5]. On the other hand, RFA, a minimally invasive surgical alternative, aims to eradicate tumor lesions directly [6].

In recent times, integrating TACE with RFA has been considered advantageous, particularly for advanced HCC patients who are unable to pursue surgical routes. Notwithstanding, the long-term survival and quality of life of these patients receiving this combined treatment regimen remains under-explored. This study aims to fill this gap by conducting a thorough retrospective analysis of the clinical data of 125 liver cancer patients, treated in our hospital from January 2020 to December 2021. We aim to probe the efficacy of this combined TACE and RFA regimen in enhancing the patient outcome, compare the overall survival rates, and evaluate complication rates, recurrence rates, and quality of life, thereby providing a robust reference for future treatment plans in clinical settings.

Materials and Methods

Study Population

A total of 125 patients with liver cancer admitted to our hospital from January 2020 to December 2021 were included in this retrospective analysis. The patients were divided into two groups: the monotherapy group (63 patients) and the combination group (62 patients), based on different treatment approaches. The inclusion criteria were as follows: (1) with diagnosis of advanced-stage liver cancer through imaging examinations, tumor biomarker tests, and patho-

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logical examinations; (2) receiving subsequent treatment at our hospital; (3) not eligible for curative surgery; and (4) with complete clinical data available. The exclusion criteria were as follows: (1) diffuse liver cancer; (2) presence of portal vein metastasis or hepatic vein metastasis; (3) contraindications to radiofrequency ablation (RFA) or transcatheter arterial chemoembolization (TACE); (4) concurrent other malignant tumors; (5) inappropriate timing for treatment due to cardiovascular events or acute exacerbation of various chronic diseases; and (6) presence of immune system disorders or dysfunction. This study was approved by the ethics committee of Affiliated Hospital of Hebei University (Approval no. ERC2024085V7). Signed written informed consents were obtained from the patients and guardians.

Intervention Measures

Monotherapy Group

Patients in the monotherapy group received TACE. The procedure involved routine disinfection of the puncture site, Seldinger technique for percutaneous femoral artery puncture, placement of a catheter sheath, digital subtraction angiography to visualize the main blood supply artery of the tumor, and catheter insertion followed by contrast agent injection. The vascular distribution within the lesion was carefully observed. A chemotherapy drug combination of pirarubicin (20–30 mg), cisplatin (80 mg), and iodized oil (5–15 mL) was then administered through the catheter, followed by embolization of the distal artery using gelatin sponge. Digital subtraction angiography was performed again after treatment to evaluate the blood supply of the tumor. If necessary, one additional session of TACE was performed at a 4-week interval, with a total of 1–3 treatments depending on the patient's condition. The digital angiography system used for treatment was the Artis pheno (NMPA20183060137), manufactured by Siemens Healthineers (Shanghai, China).

Combination Group

In addition to the procedures performed in the monotherapy group, patients in the combination group underwent RFA after one session of TACE. The RFA procedure was as follows: preoperative imaging examinations were conducted to determine the location of the lesion and the puncture point and pathway. A radiofrequency needle was used to puncture the lesion, and the electrode was activated to cover the entire lesion and a surrounding area of approximately 1.0 cm. The radiofrequency parameters were adjusted according to the characteristics of the tumor, typically with a treatment power of 80–100 W and a central temperature maintained at 90–110 °C. The treatment time for each lesion was $\geq$20 min. The device used was a multi-level radiofrequency tumor ablation instrument, model RFA-I (NMPA20173014194), developed by Bolai Optoelectronic Technology Development Company, Beijing, China. After the procedure, the puncture channel was ablated. If necessary, one additional session of RFA was performed at an after the 4-week follow-up.

Outcome Measures

Clinical efficacy: The clinical efficacy of both groups was evaluated according to the criteria for solid tumor efficacy assessment. Tumor lesions were observed through computed tomography (CT) or contrast-enhanced CT reexamination. Complete remission was defined as the complete disappearance of tumor lesions and the absence of any lesions for at least 4 weeks. Partial remission was defined as a decrease in the sum of tumor lesion radii by $\geq$30% for at least 4 weeks. Disease stability was defined as a decrease in the sum of tumor lesion radii by $<$30% or an increase by $<$20%. Disease progression was defined as an increase in the sum of tumor lesion radii by $\geq$20% or the occurrence of new or metastatic tumors [7]. The overall response rate (%) was calculated as the number of cases with complete remission or partial remission divided by the total number of cases, multiplied by 100%.

Liver function indicators: The levels of liver function indicators, including serum alanine aminotransferase, aspartate aminotransferase, albumin, and total bilirubin, were measured using a fully automated biochemical analyzer before the procedure and 4 weeks after the procedure in both groups.

Tumor markers: The levels of tumor markers, including carcinoembryonic antigen (CEA), epidermal growth factor receptor (EGFR), and alpha-fetoprotein (AFP), were compared before the procedure and 4 weeks after the procedure in both groups. CEA and EGFR were measured using enzyme-linked immunosorbent assay, while AFP was measured using a double antibody sandwich method.

Complications: The occurrence of complications, such as liver function impairment, digestive system reactions, and bone marrow suppression, was compared between the two groups before discharge.

Quality of life: The quality of life of the two groups was assessed before treatment and at 1-year follow-up using a concise health status questionnaire. The questionnaire evaluated eight dimensions of physical function, social function, physical role function, mental health, bodily pain, emotional function, vitality, and general health. Scores ranged from 0 to 100, with higher scores indicating better quality of life [8].

Prognosis: Patients underwent monthly follow-up examinations for the first three months postoperatively, followed by examinations every six months for the next three years, and annual examinations thereafter. The prognosis of both groups, including recurrence rate and survival rate, was recorded.

Table 1. Comparison of general information between the two groups.

Group	Sample size	Gender (n, %)		Age (years)	Tumor diameter (cm)	Child-Pugh liver function classification (n, %)	
		Male	Female			A	B
Combination group	62	39 (62.90)	23 (37.10)	58.65 ± 6.32	4.15 ± 0.32	50 (80.65)	12 (19.35)
Single group	63	38 (60.32)	25 (39.68)	58.90 ± 6.45	4.20 ± 0.28	52 (82.54)	11 (17.46)
χ^2/t		0.088		0.219	0.930	0.075	
p		0.766		0.827	0.354	0.785	

Table 2. Comparison of clinical efficacy between the two groups.

Group	Sample size	Complete remission (n, %)	Partial remission (n, %)	Disease stable (n, %)	Disease progression (n, %)	Overall response rate (n, %)
Combination group	62	19 (30.65)	28 (45.16)	12 (19.35)	3 (4.84)	47 (75.81)
Single group	63	17 (26.98)	18 (28.57)	24 (38.10)	4 (6.35)	35 (55.56)
χ^2						5.679
p						0.017

Statistical Methods

Data analysis was performed using Statistic Package for Social Science (SPSS) 25.0 statistical software (IBM, Armonk, NY, USA). Count data were expressed as [n (%)] and analyzed using the chi-squared test. After we tested the normality of the data using the Shapiro–Wilk test, normally distributed measurement data were presented as mean ± standard deviation ($\bar{x} \pm s$) and analyzed using the *t*-test. A *p*-value of <0.05 was considered statistically significant.

Results

Comparison of General Information between the Two Groups

As shown in Table 1, there were no statistically significant differences in gender, age, tumor diameter, and Child-Pugh liver function classification between the two groups ($p > 0.05$), indicating comparability between the groups.

Comparison of Clinical Efficacy between the Two Groups

As presented in Table 2, the combination group had a higher total effective rate than the control group, with a statistically significant difference ($p < 0.05$), suggesting that transcatheter arterial chemoembolization combined with radiofrequency ablation can improve the clinical efficacy in patients with liver cancer.

Comparison of Liver Function Indexes before and after Surgery between the Two Groups

Table 3 shows that there were no statistically significant differences ($p > 0.05$) in the preoperative levels of alanine aminotransferase, aspartate aminotransferase, albumin, and total bilirubin between the two groups. However, the postoperative levels of alanine aminotransferase, aspartate aminotransferase, and total bilirubin in the combination group were lower than those in the single-group, while the albumin level was significantly higher in the combination group, with statistically significant differences ($p < 0.05$). This suggests that transcatheter arterial chemoembolization combined with radiofrequency ablation can alleviate liver function damage in patients with liver cancer.

Comparison of Serum Tumor Marker Levels before and after Surgery between the Two Groups

As shown in Table 4, there were no statistically significant differences ($p > 0.05$) in the preoperative levels of carcinoembryonic antigen, alpha-fetoprotein, and epidermal growth factor receptor (EGFR) between the two groups. However, the postoperative levels of these serum tumor markers in the combination group were lower than those in the single-group, with statistically significant differences ($p < 0.05$). This indicates that transcatheter arterial chemoembolization combined with radiofrequency ablation can reduce the serum tumor marker levels in patients with liver cancer.

Comparison of Incidence of Complications between the Two Groups

The incidence of complications such as liver function damage, digestive system reactions, and bone marrow suppression in the combination group was lower than that in the single-group, with a statistically significant difference ($p < 0.05$). This suggests that transcatheter arterial chemoembolization combined with radiofrequency ablation can reduce the occurrence of complications in patients with liver cancer (Table 5).

Comparison of Quality of Life Scores between the Two Groups

As shown in Tables 6,7, there were no statistically significant differences ($p > 0.05$) in the quality of life scores regarding physical function, social function, physiological role, mental health, bodily pain, emotional role, vitality, and overall health between the two groups upon discharge. However, the combination group had higher scores in all aspects of quality of life compared to the single-group at

Table 3. Comparison of liver function indicators before and after surgery in the two groups.

Group	n	ALT (U/L)		AST (U/L)		Albumin (g/L)		Total bilirubin (μmol/L)	
		Before surgery	4 weeks after surgery*	Before surgery	4 weeks after surgery*	Before surgery	4 weeks after surgery*	Before surgery	4 weeks after surgery*
Combination group	62	389.74 ± 30.56	91.62 ± 20.45	360.84 ± 25.78	85.38 ± 15.22	25.10 ± 3.14	37.65 ± 4.30	53.95 ± 3.70	24.46 ± 2.10
Single group	63	390.10 ± 31.15	168.74 ± 22.32	361.25 ± 26.50	161.34 ± 18.35	24.86 ± 3.20	32.34 ± 3.65	54.11 ± 4.02	35.60 ± 3.02
t		0.065	20.133	0.088	6.902	0.423	7.447	0.231	23.908
p		0.948	0.001	0.930	0.001	0.673	0.001	0.817	0.001

(*: The parameter had significant difference). ALT, Alanine aminotransferase; AST, Aspartate aminotransferase.

Table 4. Comparison of serum tumor marker levels before and after surgery in two groups.

Group	n	Carcinoembryonic antigen (ng/mL)		Alpha-fetoprotein (ng/mL)		Epidermal growth factor receptor (μg/L)	
		Before surgery	4 weeks after surgery*	Before surgery	4 weeks after surgery*	Before surgery	4 weeks after surgery*
Combination group	62	15.98 ± 1.74	8.95 ± 1.04	209.54 ± 20.32	76.12 ± 8.75	61.96 ± 8.72	11.90 ± 3.15
Single group	63	16.04 ± 1.80	11.25 ± 1.32	210.15 ± 21.14	131.56 ± 14.18	62.04 ± 9.05	20.88 ± 3.62
t		0.189	10.810	0.164	26.256	0.050	14.786
p		0.850	<0.001	0.870	<0.001	0.960	<0.001

(*: The parameter had significant difference).

Table 5. Comparison of complication incidence between two groups.

Group	Number of cases	Hepatic dysfunction	Gastrointestinal reactions	Bone marrow suppression	Total
Combination group	62	1 (1.61)	2 (3.23)	0 (0.00)	3 (4.84)
Single group	63	4 (6.35)	4 (6.35)	3 (4.76)	11 (17.46)
χ^2					5.005
p					0.025

Table 6. Comparison of quality of life scores between two groups.

Group	Number of cases	Physical function		Social function		Physiological function		Mental health	
		Pre-discharge	1-year follow-up	Pre-discharge	1-year follow-up	Pre-discharge	1-year follow-up	Pre-discharge	1-year follow-up
Combination group	62	50.90 ± 6.52	75.42 ± 7.66	51.28 ± 6.30	75.86 ± 7.45	52.32 ± 6.44	76.40 ± 7.30	58.56 ± 6.80	77.90 ± 7.50
Single group	63	50.80 ± 6.72	66.50 ± 7.50	51.50 ± 6.52	70.76 ± 6.52	52.75 ± 6.76	71.25 ± 7.18	59.14 ± 6.74	72.30 ± 7.22
t		0.084	6.578	0.192	4.075	0.364	3.976	0.476	4.253
p		0.933	0.001	0.848	0.001	0.716	0.001	0.633	0.001

Table 7. Comparison of health-related quality of life scores between two groups.

Group	Number of cases	Physical pain		Emotional function		Vitality		General health	
		Pre-discharge	1-year follow-up	Pre-discharge	1-year follow-up	Pre-discharge	1-year follow-up	Pre-discharge	1-year follow-up
Combination group	62	52.26 ± 5.50	72.54 ± 6.20	53.35 ± 5.74	73.95 ± 6.32	51.32 ± 5.26	74.50 ± 6.70	51.82 ± 5.76	73.24 ± 6.95
Single group	63	51.90 ± 5.86	66.40 ± 6.38	53.58 ± 5.80	68.76 ± 6.14	51.60 ± 5.38	67.30 ± 6.62	51.90 ± 5.80	68.86 ± 6.50
t		0.313	5.455	0.223	4.657	0.294	6.043	0.077	3.640
p		0.755	0.001	0.824	0.001	0.769	0.001	0.938	0.001

Table 8. Comparison of prognosis between the two groups.

Group	Number of cases	Recurrence rate	One-year survival rate
Combination group	62	12 (19.35%)	58 (93.55%)
Single group	63	32 (50.79%)	42 (66.67%)
χ^2		13.541	14.113
p		0.001	0.001

the one-year follow-up ($p < 0.05$). This indicates that transcatheter arterial chemoembolization combined with radiofrequency ablation can improve the quality of life in patients with liver cancer.

Comparison of Prognosis between the Two Groups

The recurrence rate in the combination group was 19.35% (12/62), which was lower than the rate of 50.79% (32/63) in the single-group, with a statistically significant difference ($\chi^2 = 13.541$, $p = 0.001$). The one-year survival rate in the combination group was 93.55% (58/62), which was higher than the rate of 66.67% (42/63) in the single-group, with a statistically significant difference ($\chi^2 = 14.113$, $p = 0.001$). These findings indicate that transcatheter arterial chemoembolization combined with radiofrequency ablation can decrease the recurrence rate and improve the one-year survival rate in patients with liver cancer (Table 8).

Discussion

Hepatocellular carcinoma (HCC) is a major malignant tumor that poses a serious threat to human health and life, with 1–1.5 million new cases reported worldwide annually [9]. As a country with high HCC incidence, China accounts for 45% of total global cases, ranking HCC as the second most common malignancy in China [10, 11]. In recent years, with the gradual development and improvement of interventional and minimally invasive technologies, significant progress has been made in the treatment of HCC at all stages [12, 13].

The liver is supplied by dual blood sources—the portal vein and hepatic artery—with the portal vein providing the majority of the blood supply. However, HCC lesions are predominantly supplied by the hepatic artery. Therefore, blocking the hepatic arterial blood supply is key for treatment [14]. Transcatheter arterial chemoembolization (TACE) is a common interventional treatment for HCC that infuses chemotherapeutic agents into the major feeding arteries of HCC lesions to achieve tumor blood supply blockade and cancer cell killing [15, 16]. However, clinical application has revealed that TACE alone can upregulate the expression of pro-angiogenic factors in HCC tissue, actively establish collateral circulation, and result in incomplete embolization post-procedure, leading to high recurrence and metastasis rates in patients [17]. Radiofrequency ablation (RFA) is a minimally invasive surgical technique that uses radiofrequency to produce thermal injury and necrosis in the tumor, providing a more direct and definitive elimination of cancerous tissue. However, the efficacy of RFA is affected by many factors including tumor size, number, and vascular invasion status [18]. RFA alone has difficulty completely ablating larger tumors, thus exhibiting certain limitations when used alone. The aforementioned two treatments have some flaws and limitations when used separately, while combined application can achieve better therapeutic effects [19]. TACE blocks tumor blood supply, reduces heat sink effect, and establishes a good foundation for subsequent RFA to achieve more ideal outcomes [20]. Meanwhile, the iodized oil used in TACE can aid thermal conduction during RFA to improve heating efficacy and more effectively eradicate cancer cells. Therefore, RFA after TACE allows the two treatments to complement each other's advantages and improve efficacy [21].

A study by Fang *et al*. [22] found that the total effective rate of TACE combined with RFA for HCC was 78.57%, significantly higher than 50.00% with TACE alone ($p < 0.05$). Our study demonstrates that the total effective rate was 75.81% in the combination group, markedly higher than 55.56% in the monotherapy group ($p < 0.05$), consistent with the aforementioned findings and indicating superior effects of the combined approach. This is attributable to the additional thermal injury induced by RFA to directly and definitively destroy cancerous tissue and improve patient outcomes. At 4 weeks post-procedure, the combination group had lower alanine aminotransferase, aspartate aminotransferase, total bilirubin, and higher albumin compared to the monotherapy group ($p < 0.05$), suggesting that the combined treatment could mitigate liver function impairment. TACE infuses chemotherapeutic agents into major HCC feeding arteries and embolizes them to induce ischemic necrosis of cancer cells. However, TACE efficacy alone depends on lesion blood supply and can result in incomplete embolization, leading to large variances in chemotherapeutic effects post-infusion. Collateral circulation may also develop after embolization and affect tumor blood supply blockade, especially in middle-late stage HCC patients who require 1–3 TACE sessions and consequently large cumulative chemotherapeutic doses that damage liver function. The addition of RFA produces a synergistic effect, reduces the number of embolization procedures required, and thus alleviates liver function injury. At 4 weeks post-procedure, the combination group had lower carcinoembryonic antigen, alpha-fetoprotein, and epidermal growth factor receptor compared to the monotherapy group ($p < 0.05$), indicating a better reduction in serum tumor markers with the combined approach. This is because TACE blocks tumor blood supply, reduces the heat sink effect, and establishes a good foundation for subsequent effective RFA. Meanwhile, the iodized oil used in TACE aids RFA thermal conduction and improves heating efficacy to more effectively eradicate cancer cells and reduce serum tumor marker levels. A study by Cun *et al*. [23] found lower complication rates with TACE plus RFA compared to TACE alone for HCC treatment. The combination group also exhibited a lower incidence of liver function impairment, gastrointestinal reactions, and bone marrow suppression relative to the monotherapy group ($p < 0.05$), consistent with the aforementioned findings and indicating the combined treatment can reduce complications. This is attributable to the interventional nature of TACE which embolizes tumors and blocks feeding arteries using iodized oil emulsion, causing

minimal damage to liver tissue, while RFA is a minimally invasive technique that effectively treats tumors with minimal damage to patients and protects surrounding normal tissue to reduce injury and complications. According to Zhao *et al*. [24], RFA can achieve curative treatment for HCC $\leq$3 cm^3, but residual tumors may exist for larger lesions. Some researchers believe that performing RFA after blocking tumor blood supply can increase complete tumor necrosis rates, and the combined TACE and RFA approach has been clinically validated for HCC treatment, although reported prognosis outcomes remain inconsistent [13, 25, 26]. In our study, the combination group had lower recurrence rates and higher 1-year survival compared to the monotherapy group ($p < 0.05$). This is likely because TACE can block the abundant arterial and arteriovenous blood supplies of HCC lesions, mitigating RFA peri-ablation blood flow cooling effects and facilitating increased RFA electrode temperatures. After TACE, a tumor capsule forms that concentrates RFA heat within the tumor region and prevents outward thermal dissipation, thereby improving tumor necrosis rates and patient prognosis.

However, this study had several limitations. Firstly, we only included patients from a single hospital, which may make our findings not applicable to other regions. Secondly, the small sample size of our study may have caused some bias in our results. More multicenter, large sample prospective studies will be conducted in the future to further validate our findings.

Conclusions

In summary, TACE combined with RFA demonstrates ideal therapeutic efficacy for HCC, relieves liver function impairment, reduces serum tumor marker levels, lowers postoperative complications, improves quality of life, and enhances prognosis. Consequently, this combined treatment approach is endorsed for clinical practice.

Availability of Data and Materials

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

Author Contributions

SFL, FZ, MS, HSW, JTB, and LZ designed the research study. SFL and FZ performed the research. MS and HSW provided help and advice on the clinical data collection and analysis. JTB analyzed the data. LZ supervised the project and provided critical feedback. SFL and LZ wrote the article. All authors revised the manuscript critically for important intellectual content. 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.

Ethics Approval and Consent to Participate

This study was approved by the ethics committee of Affiliated Hospital of Hebei University (Approval no. ERC2024085V7) and was conducted in accordance with the principles of the Declaration of Helsinki. Signed written informed consent were obtained from the patients and guardians.

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Conflict of Interest

The authors declare no conflict of interest.

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