



Retrospective Study

Drug-eluting beads chemoembolization combined with programmed cell death 1 inhibitor and lenvatinib for large hepatocellular carcinoma

Hui Yang, Guang-Ping Qiu, Jie Liu, Tie-Quan Yang

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Hui Yang, Guang-Ping Qiu, Jie Liu, Tie-Quan Yang, Department of Interventional Therapy, Ningbo No. 2 Hospital, Ningbo 315000, Zhejiang Province, China

Corresponding author: Tie-Quan Yang, BMed, Attending Doctor, Department of Interventional Therapy, Ningbo No. 2 Hospital, No. 41 Xibei Road, Ningbo 315000, Zhejiang Province, China. younghc5@163.com

Abstract

BACKGROUND

The combination of transarterial chemoembolization (TACE), lenvatinib, and programmed cell death 1 (PD-1) inhibitor has been widely used in the treatment of advanced hepatocellular carcinoma (HCC) and has achieved promising results. However, there are few studies comparing whether drug-eluting beads TACE (D-TACE) can bring more survival benefits to patients with large HCC compared to conventional TACE (C-TACE) in this triplet therapy.

AIM

To compare the efficacy and adverse events (AEs) of triple therapy comprising D-TACE, PD-1 inhibitors, and lenvatinib (D-TACE-P-L) and C-TACE, PD-1 inhibitors, and lenvatinib (C-TACE-P-L) in patients with large HCC (maximum diameter ≥ 5 cm), and analyze the prognostic factors.

METHODS

Following a comprehensive review of our hospital's medical records, this retrospective study included 104 patients: 50 received D-TACE-P-L, and 54 received C-TACE-P-L. We employed Kaplan-Meier estimation to assess the median progression-free survival (PFS) between the two groups, utilized Cox multivariate regression analysis to identify prognostic factors, and applied the χ^2 test to evaluate AEs.

RESULTS

The objective response rate (ORR) and median PFS were significantly higher in the D-TACE-P-L group compared to the C-TACE-P-L group (ORR: 66.0% vs 44.4%, $P = 0.027$; median PFS: 6.8 months vs 5.0 months, $P = 0.041$). Cox regression analysis identified treatment option, portal vein tumor thrombus, and hepatic vein invasion as protective factors for PFS. AEs were comparable between the two

groups.

CONCLUSION

D-TACE-P-L may have significantly better PFS and ORR for large HCC, while exhibiting similar AEs to C-TACE-P-L.

Key Words: Large hepatocellular carcinoma; Conventional transarterial chemoembolization; Drug-eluting beads transarterial chemoembolization; Programmed cell death 1 inhibitor; Lenvatinib

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Core Tip: A retrospective analysis encompassing 104 patients diagnosed with large hepatocellular carcinoma (≥ 5 cm), focused on comparing the efficacy and safety of two treatment modalities, which were the triple combination therapy of drug-eluting beads transarterial chemoembolization (D-TACE), programmed cell death 1 inhibitor, and lenvatinib (D-TACE-P-L) and the triple therapy consisting of conventional TACE, programmed cell death protein 1 inhibitor, and lenvatinib. Progression-free survival, tumor response, and adverse events were compared between the two groups, and the findings revealed that D-TACE-P-L demonstrated significantly superior median progression-free survival and objective response rate, while maintaining comparable toxicity profiles. Based on these outcomes, this study proposed that the D-TACE-P-L therapy served as a preferential treatment option for individuals suffering from large hepatocellular carcinoma.

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INTRODUCTION

Hepatocellular carcinoma (HCC) ranks as the sixth most prevalent cancer worldwide and is associated with a poor prognosis. Notably, Chinese patients constitute approximately half of the global HCC caseload[1,2]. Due to insidious onset and rapid progression, large lesions, defined as having a maximum diameter exceeding 5 cm, are frequently diagnosed at an advanced stage, rendering them ineligible for surgical resection[3].

Currently, transarterial chemoembolization (TACE) is a widely adopted technique for managing unresectable HCC (uHCC)[4]. However, conventional TACE (C-TACE), which employs lipiodol mixed with chemotherapeutic agents, demonstrates limited efficacy in treating large HCC lesions. The objective response rate (ORR) ranges from 16% to 29%, while overall survival (OS) is restricted to between 6.5 and 9.9 months[5-7]. In contrast, drug-eluting beads TACE (D-TACE) offers sustained drug release alongside persistent embolization, potentially enhancing treatment outcomes for HCC[8]. For large or massive HCC tumors, D-TACE has been shown to achieve higher ORR rates, longer progression-free survival (PFS), and fewer adverse reactions compared to C-TACE[9,10]. Nevertheless, monotherapy with TACE remains inadequate regarding effectiveness; local recurrence rates at three months, six months, and one year are reported to be 18.6%, 33.4%, and 61.8%, respectively[11]. The TACE procedure induces a hypoxic environment within residual tumor tissue that stimulates increased production of vascular endothelial growth factor, leading to neovascularization - a significant contributor to tumor recurrence post-TACE. Furthermore, TACE does not effectively counteract immune evasion by tumor cells.

In recent years, substantial advancements have been made in systemic therapies for HCC encompassing tyrosine kinase inhibitors (TKIs) and immune checkpoint inhibitors. TKIs have demonstrated efficacy in inhibiting tumor vessel proliferation while improving median OS among patients with HCC; thus, sorafenib and lenvatinib are recommended as first-line TKIs for uHCC management[12,13]. Immunotherapy has the potential to effectively inhibit the immune evasion mechanisms employed by tumor cells. Although immunotherapy alone has not exhibited superior efficacy relative to traditional treatments for HCC on its own merit, numerous studies indicate that combining TKIs with programmed cell death 1 (PD-1) inhibitors yields improved outcomes for patients suffering from this malignancy[14-18].

Therapies that inhibit angiogenesis, such as antibodies directed against vascular endothelial growth factor or TKIs, may postpone the revascularization and recurrence of tumors following TACE. PD-1 inhibitors can limit immune evasion, thereby enhancing the immune response to kill tumor cells. Due to their synergistic effect, combined therapy with TACE, PD-1 inhibitors, and lenvatinib has been proven to have better efficacy in treating uHCC[13,19]. However, the efficacy of combined therapy with C-TACE, PD-1 inhibitors, and lenvatinib (C-TACE-P-L) for treating large HCC remains unsatisfactory. D-TACE combined with PD-1 inhibitor and lenvatinib (D-TACE-P-L) may be better than C-TACE-P-L. Current available clinical studies on the utilization of D-TACE-P-L for large HCC are scarce, reflecting the need for further investigations and clinical trials to fully assess its potential benefits and risks in this specific patient population. Consequently, this retrospective study aimed to evaluate and compare the efficacy and safety of these two therapies in patients with large HCC.

MATERIALS AND METHODS

Patient criteria

Our research strictly adhered to the ethical principles outlined in the Declaration of Helsinki. The ethics committee of Ningbo No. 2 Hospital conducted a thorough review of our study and granted its approval. Since this study was conducted retrospectively, the ethics committee waived the necessity for informed consent. Furthermore, data were collected and analyzed anonymously to ensure participant privacy and confidentiality. Data were obtained from a cohort of patients with large HCC who received either D-TACE-P-L or C-TACE-P-L between May 1, 2019, and December 1, 2022. The inclusion criteria for our study included: (1) Age between 18-75 years; (2) Diagnosis of HCC confirmed by pathological examination; (3) Treatment with either D-TACE-P-L or C-TACE-P-L; and (4) Presence of at least one measurable lesion that exhibited arterial enhancement, with the largest lesion exceeding 5 cm in diameter. Patients meeting any of the following exclusion criteria were excluded: (1) Eastern Cooperative Oncology Group Performance Status score > 1; (2) Receipt of other anticancer treatments; (3) Concurrent Child-Pugh grade C status; (4) Presence of other malignancies; or (5) Incomplete medical records or information. Magnetic resonance imaging (MRI), or contrast-enhanced computed tomography (CT), was performed within one week prior to initial treatment, along with all necessary laboratory tests completed within three days.

Treatment

All patients received intravenous injections of PD-1 inhibitors, including tislelizumab (200 mg), sintilimab (200 mg), toripalimab (240 mg), and camrelizumab (200 mg) every three weeks. Additionally, they were administered lenvatinib orally at a standard dose of 8 mg for those weighing less than 60 kg or 12 mg for those weighing 60 kg or more, or an individualized dose as appropriate. Furthermore, TACE procedures were performed every one to two months if enhanced CT or MRI indicated significant arterial blood supply to the tumor; PD-1 inhibitors and lenvatinib were withheld three days prior to and following TACE. Digital subtraction angiography was utilized to identify arteries supplying blood to the tumor during TACE. Subsequently, a microcatheter was inserted into these arteries based on patient preference for either D-TACE or C-TACE. Drug-eluting beads or iodized oil containing doxorubicin (20 mg in C-TACE and 50 mg in D-TACE) were then slowly injected through the microcatheters for embolization. The efficacy of embolization was assessed *via* digital subtraction angiography, with the procedure concluded upon achieving satisfactory results.

Evaluation criteria

According to the mRECIST criteria, lesions were classified as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD)[20]. The primary objectives were to assess the median PFS, ORR, disease control rate (DCR), and prognostic factors of PFS. The ORR was defined as the incidence of CR and PR. The DCR was defined as the incidence of CR, PR, or SD. PFS was defined as the duration from the first TACE session to the occurrence of PD, death, or the last day of follow-up. Additionally, we aimed to evaluate adverse events (AEs) as secondary outcomes. AEs were evaluated and graded according to the National Cancer Institute's Common Terminology Criteria for Adverse Events (version 4.0).

Follow-up

Patients were monitored at intervals of 1 to 3 months following their initial TACE. During each follow-up visit, a comprehensive evaluation was performed, which included hematological and biochemical tests as well as contrast-enhanced CT or MRI scans. If the lesion was classified as PD or if the patient could not tolerate treatment, the original therapy was discontinued, and alternative appropriate treatment options were considered for these patients. The follow-up endpoint was established as May 1, 2024.

Statistical analyses

Categorical variables are presented as percentages and analyzed using the χ^2 test. Continuous variables are reported as means \pm standard deviations and compared with the Student's *t*-test. The median PFS between the two groups was assessed using Kaplan-Meier estimation. We assessed clinical characteristics through Cox univariate analysis. The items that exhibited statistical significance ($P < 0.1$) were assessed again using Cox multivariate regression to uncover prognostic factors of PFS ($P < 0.05$). Other statistically significant differences were defined as those for which $P < 0.05$. All the statistical analyses were performed using SPSS Statistics version 24.3.

RESULTS

Patient characteristics

After reviewing the medical records of our hospital, we identified 178 patients with large HCC who received either D-TACE-P-L or C-TACE-P-L, meeting the inclusion criteria. A total of 74 patients were excluded based on the predefined exclusion criteria, as illustrated in [Figure 1](#). Ultimately, our study included 104 patients: 50 in the D-TACE-P-L group and 54 in the C-TACE-P-L group. There were four categories of PD-1 inhibitors utilized: Tislelizumab for 14 patients (13.5%), sintilimab for 17 patients (16.3%), camrelizumab for 45 patients (43.3%), and toripalimab for 17 patients (26.9%). No statistically significant differences were observed in baseline characteristics ([Table 1](#)).

Table 1 Baseline characteristics of the patients

Characteristic	D-TACE-P-L group (n = 50)	C-TACE-P-L group (n = 54)	P value
Sex, n (%)			0.564
Male	42 (84.0)	43 (79.6)	
Female	8 (16.0)	11 (20.4)	
Age (years), mean ± SD	60.8 ± 9.2	62.2 ± 9.4	0.443
ECOG PS, n (%)			0.252
0	14 (28.0)	10 (18.5)	
1	36 (72.0)	44 (81.5)	
Child-Pugh class, n (%)			0.561
A	26 (52.0)	25 (46.3)	
B	24 (48.0)	29 (53.7)	
BCLC, n (%)			0.556
B	14 (28.0)	18 (33.3)	
C	36 (72.0)	36 (66.7)	
AFP, n (%)			0.727
≤ 400 ng/mL	23 (46.0)	23 (42.6)	
> 400 ng/mL	27 (54.0)	31 (57.4)	
Number of tumors, n (%)			0.392
≤ 3	31 (62)	29 (53.7)	
> 3	19 (38)	25 (46.3)	
Largest tumor size (mm), mean ± SD	96.3 ± 27.7	91.0 ± 36.7	0.324
PVTT, n (%)			0.873
No	23 (46.0)	24 (44.4)	
Yes	27 (54.0)	30 (55.6)	
Hepatic vein invasion, n (%)			0.656
No	38 (76.0)	43 (20.4)	
Yes	12 (24.0)	11 (79.6)	
Extrahepatic metastasis, n (%)			0.661
No	41 (82.0)	46 (85.2)	
Yes	9 (18.0)	8 (14.8)	
Number of TACE, mean ± SD	2.46 ± 1.0	2.56 ± 1.1	0.640

C-TACE-P-L: Conventional transarterial chemoembolization combined with lenvatinib plus programmed cell death 1 inhibitor; D-TACE-P-L: Drug-eluting beads transarterial chemoembolization combined with lenvatinib plus programmed cell death 1 inhibitor; ECOG PS: Eastern Cooperative Oncology Group Performance Status; BCLC: Barcelona Clinic Liver Cancer; AFP: Alpha-fetoprotein; PVTT: Portal vein tumor thrombus; TACE: Transarterial chemoembolization.

Tumor response

The tumor response and DCR were comparable between the two groups, with no significant differences observed ($P = 0.113$, $P = 0.143$; Table 2). However, a significant difference in ORR was noted between the groups (66.0% vs 44.4%, $P = 0.027$). In the D-TACE-P-L group, the percentages of CRs and PRs were 18.0% and 48.0%, whereas in the C-TACE-P-L group, these percentages were 7.4% and 37.0%. No significant differences were found among the various PD-1 inhibitor subgroups ($P = 0.927$; Table 3).

PFS and analysis of its prognostic factors

The D-TACE-P-L group exhibited a superior median PFS of 6.8 months [95% confidence interval (CI): 4.45-9.15] compared to that of the C-TACE-P-L group, which had a median PFS of 5.0 months (95%CI: 4.314-5.753). The hazard ratio

Table 2 Tumor response, *n* (%)

Tumor response	D-TACE-P-L	C-TACE-P-L	<i>P</i> value
CR	9 (18.0)	4 (7.4)	0.113
PR	24 (48.0)	20 (37.0)	
SD	12 (24.0)	19 (35.2)	
PD	5 (10.0)	11 (20.4)	
ORR (CR + PR)	33 (66.0)	24 (44.4)	0.027
DCR (CR + PR + SD)	45 (90.0)	43 (81.0)	0.143

C-TACE-P-L: Conventional transarterial chemoembolization combined with lenvatinib plus programmed cell death 1 inhibitor; D-TACE-P-L: Drug-eluting beads transarterial chemoembolization combined with lenvatinib plus programmed cell death 1 inhibitor; CR: Complete response; PR: Partial response; SD: Stable disease; PD: Progressive disease; ORR: Objective response rate; DCR: Disease control rate.

Table 3 Tumor response of different programmed cell death 1 inhibitor groups, *n* (%)

PD-1 inhibitor	CR	PR	SD	PD	<i>P</i> value
Tislelizumab	2 (14.3)	5 (35.7)	4 (28.6)	3 (24.1)	0.927
Sintilimab	1 (5.9)	10 (58.8)	5 (29.4)	1 (5.9)	
Camrelizumab	6 (13.3)	17 (37.8)	14 (31.1)	8 (17.8)	
Toripalimab	4 (14.3)	12 (42.9)	8 (28.5)	4 (14.3)	

PD-1: Programmed cell death 1; CR: Complete response; PR: Partial response; SD: Stable disease; PD: Progressive disease.

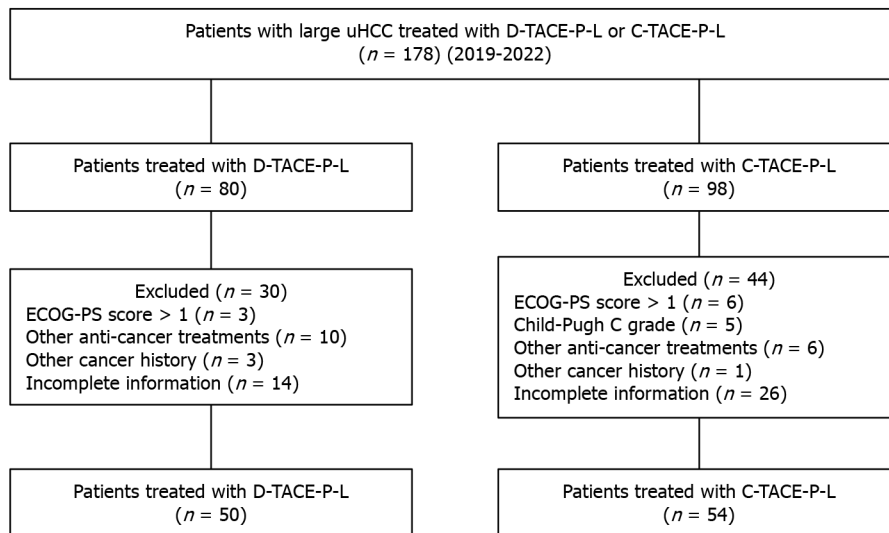


Figure 1 Selection criteria. uHCC: Unresectable hepatocellular carcinoma; C-TACE-P-L: Conventional transarterial chemoembolization combined with lenvatinib plus programmed cell death 1 inhibitor; D-TACE-P-L: Drug-eluting beads transarterial chemoembolization combined with lenvatinib plus programmed cell death 1 inhibitor; ECOG-PS: Eastern Cooperative Oncology Group Performance Status.

(HR) was 1.422, with a 95%CI of 0.961-2.104, indicating a statistically significant difference (Figure 2, *P* = 0.041). Cox regression analysis (as detailed in Table 4) revealed the following prognostic factors for PFS: Portal vein tumor thrombus (PVTT) (No/Yes, HR = 1.670; 95%CI: 1.120-2.491; *P* = 0.012), hepatic vein invasion (No/Yes, HR = 1.807; 95%CI: 1.105-2.956; *P* = 0.018), and treatment option (D-TACE-P-L/C-TACE-P-L, HR = 1.536; 95%CI: 1.028-2.293; *P* = 0.036).

AEs

We summarized AEs in both groups (Table 5) and found that the most common AEs were fatigue (48.0% vs 37.0%), anorexia and nausea (52.0% vs 55.6%), rash (38% vs 46.3%), fever (92.0% vs 89.9%), and abdominal pain (68.0% vs 61.1%). The percentages of grade 3 AEs ranged from 0% to 12%, while no grade 4 or grade 5 AEs were observed. No statistically

Table 4 Univariate and multivariate analyses of risk factors for progression-free survival

Factors	Univariate analysis			Multivariate analysis		
	HR	95%CI	P value	HR	95%CI	P value
Sex						
Male/female	1.145	0.692-49	0.599			
Age (years)	1.007	0.987-1.027	0.495			
ECOG PS						
0/1	1.246	0.781-1.988	0.357			
Child-Pugh class						
A/B	1.301	0.881-1.921	0.185			
AFP (ng/mL)						
≤ 400/> 400	1.215	0.821-1.798	0.329			
Number of tumors						
≤ 3/> 3	1.276	0.857-1.900	0.229			
Largest tumor size (mm)	1.006	0.998-1.013	0.139			
PVTT						
No/yes	1.590	1.073-2.358	0.021	1.670	1.120-2.491	0.012
Hepatic vein invasion						
No/yes	1.621	1.012-2.596	0.044	1.807	1.105-2.956	0.018
Extrahepatic metastasis						
No/yes	1.778	1.038-3.044	0.036	1.554	0.900-2.686	0.114
Treatment option						
D-TACE-P-L/C-TACE-P-L	1.422	0.961-2.104	0.078	1.536	1.028-2.293	0.036

C-TACE-P-L: Conventional transarterial chemoembolization combined with lenvatinib plus programmed cell death 1 inhibitor; D-TACE-P-L: Drug-eluting beads transarterial chemoembolization combined with lenvatinib plus programmed cell death 1 inhibitor; ECOG PS: Eastern Cooperative Oncology Group Performance Status; AFP: Alpha-fetoprotein; PVTT: Portal vein tumor thrombus; HR: Hazard ratio; CI: Confidence interval.

significant differences emerged in either the occurrence or severity of any AEs between the two groups, indicating comparable safety profiles overall; symptomatic treatment and dose reduction proved effective in mitigating these AEs.

DISCUSSION

Iodized oil used in C-TACE consists of droplets of variable size that are prone to being washed away by blood flow, resulting in reperfusion of tumor blood vessels. In contrast, drug-eluting beads maintain a consistent size and can permanently occlude the artery supplying blood to the target tumor. Furthermore, D-TACE allows for sustained release of therapeutic agents directly into the tumor vasculature while minimizing systemic exposure. D-TACE has demonstrated efficacy and significantly reduces the incidence of AEs[21,22]. However, there remains no consensus on whether D-TACE is superior to C-TACE. Three randomized controlled trials reported varying outcomes[22-24]. Nevertheless, several studies have suggested that D-TACE may be more effective for treating large HCC[25-27]. For instance, a study conducted by Li *et al*[27] included patients with Barcelona Clinic Liver Cancer stage A/B and evaluated their response to therapy using mRECIST, revealing an ORR of 81.5% for D-TACE compared to 49.4% for C-TACE[27]. Additionally, research by Zhao *et al*[25] indicated median tumor diameters of 12.2 cm and 8.1 cm ($P < 0.005$) in the D-TACE group and C-TACE group, respectively; furthermore, both CRs and ORRs at one and three months were higher in the D-TACE group than those observed in the C-TACE group. These findings provide a foundation for our study aimed at verifying that D-TACE remains superior to C-TACE among patients with large uHCC when combined with lenvatinib and PD-1 inhibitors.

The combination therapy of TACE, lenvatinib, and PD-1 inhibitors is employed globally for the treatment of uHCC. PD-1 inhibitors function by disrupting signals that inhibit the immune system's attack on tumors, thereby enhancing the immune response against cancerous cells[17,28]. The clinical efficacy of PD-1 inhibitors can be further augmented by reducing tumor blood supply and releasing tumor-specific antigens through TACE[29,30]. However, TACE induces a

Table 5 Treatment-related adverse events in the two groups, n (%)

Adverse events	D-TACE-P-L (n = 50)		C-TACE-P-L (n = 54)		P value
	Any grade	Grade 3	Any grade	Grade 3	
Diarrhea	9 (18.0)	2 (4.0)	7 (13.0)	1 (1.8)	0.717
Hand-foot syndrome	12 (24.0)	2 (4.0)	15 (27.8)	2 (3.7)	0.882
Hypertension	13 (26.0)	1 (2.0)	14 (26.0)	0 (0.0)	0.572
Fatigue	24 (48.0)	4 (8.0)	20 (37.0)	3 (5.6)	0.522
Anorexia and nausea	26 (52.0)	4 (8.0)	30 (55.6)	5 (9.3)	0.928
Rash	19 (38.0)	1 (2.0)	25 (46.3)	3 (5.6)	0.518
Thyroid dysfunction	6 (12.0)	0 (0.0)	10 (18.5)	1 (1.8)	0.485
Hyperbilirubinemia	11 (22.0)	2 (4.0)	9 (16.7)	1 (1.8)	0.738
Fever	46 (92.0)	6 (12.0)	48 (89.9)	3 (5.6)	0.462
Abdominal pain	34 (68.0)	6 (12.0)	33 (61.1)	2 (3.7)	0.336

C-TACE-P-L: Conventional transarterial chemoembolization combined with lenvatinib plus programmed cell death 1 inhibitor; D-TACE-P-L: Drug-eluting beads transarterial chemoembolization combined with lenvatinib plus programmed cell death 1 inhibitor.

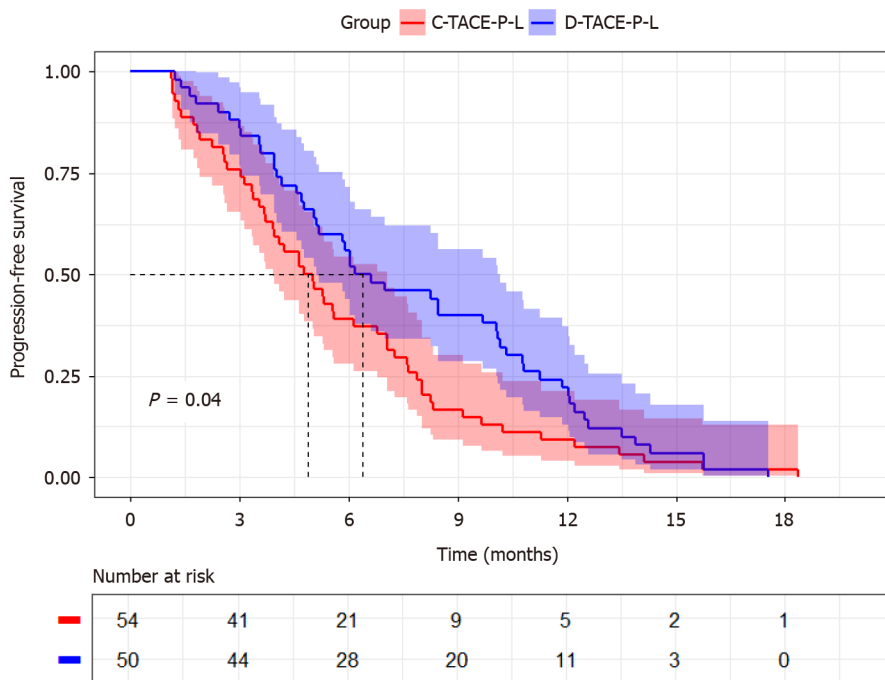


Figure 2 Kaplan-Meier curves of progression-free survival. C-TACE-P-L: Conventional transarterial chemoembolization combined with lenvatinib plus programmed cell death 1 inhibitor; D-TACE-P-L: Drug-eluting beads transarterial chemoembolization combined with lenvatinib plus programmed cell death 1 inhibitor.

hypoxic microenvironment that may lead to tumor angiogenesis, recurrence, and metastasis. Fortunately, lenvatinib has been shown to inhibit angiogenesis and counteract tumor immunosuppressive mechanisms, thus improving clinical outcomes[31]. Due to the synergistic effects of this combination therapy involving TACE, lenvatinib, and PD-1 inhibitors, patients with uHCC demonstrate improved tumor responses and survival rates. Previous research has indicated that D-TACE enhances the infiltration of immune cells in tumor tissues, whereas C-TACE decreases it[32]. It is anticipated that incorporating immune checkpoint inhibitors will enhance the therapeutic efficacy of D-TACE and potentially extend OS and PFS. Our study found that D-TACE-P-L significantly improved median PFS from 5.0 months to 6.8 months compared with C-TACE-P-L ($P = 0.041$). However, due to the short follow-up time, more than 80% of the patients are still alive. It was not feasible to assess differences in OS adequately at this time point. Additionally, while there was a statistically significant difference in ORR, no such difference was observed in DCR. More than 90% of patients experienced PD during follow-up; therefore, this duration was sufficient for evaluating ORR and DCR effectively. A larger sample size may provide more robust validation regarding differences in ORR and DCR between groups.

Overall, our experimental results align well with theoretical predictions outlined previously. However similar studies are scarce within existing literature focused on triple therapy effectiveness for treating large uHCC where tumor diameter did not serve as an inclusion criterion or prognostic factor for PFS among treatment options like D-TACE *vs* C-TACE[33, 34]. However, in one study, patients received either D-TACE or C-TACE in addition to camrelizumab[35]. The average tumor diameter (9.4 cm) in this study was significantly greater than that in other studies. The study suggested that D-TACE-C was superior to C-TACE-C in median PFS (10.0 months *vs* 3.0 months, $P = 0.017$). D-TACE-C shares similarities with D-TACE-P-L in mechanism, and enrolled participants with relatively large tumors. Thus, this similar result provides potentially relevant evidence for our outcomes. Nevertheless, further research remains essential.

Cox multivariate regression analysis identified PVTT, hepatic vein invasion, and treatment modality as independent prognostic factors for PFS. Numerous studies have corroborated that both PVTT and hepatic vein invasion serve as independent prognostic indicators for PFS, aligning with the findings of our study[33-35]. The presence of PVTT and hepatic vein invasion signifies a more advanced disease state, which is associated with poorer PFS outcomes. Furthermore, the treatment modality independently influenced prognosis, consistent with our hypothesis and reinforcing our conclusions.

Although D-TACE reduces the distribution of drugs to non-target regions, our study found no significant difference in the incidence of AEs. Similar findings have been reported in related studies[35,36]. In the investigation conducted by Ren *et al*[35], AEs included renal cell carcinoma embolization syndrome, rash, asthenia, anemia, and hypothyroidism; P values between the two groups were 0.111, 0.535, 0.484, 0.639, and 0.552, respectively, indicating no statistical significance.

However, several limitations must be acknowledged in this study. First, the retrospective design implies that treatment decisions were made by both physicians and patients, which may lead to selection bias. Additionally, the sample size was comparatively limited, highlighting the need for larger randomized controlled trials to provide more robust evidence. Finally, due to the short follow-up duration, we were unable to ascertain median OS, leaving uncertainty regarding whether D-TACE-P-L confers a superior OS compared to C-TACE-P-L.

CONCLUSION

D-TACE-P-L may have significantly better PFS and ORR for large HCC, while exhibiting similar AEs compared to C-TACE-P-L.

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FOOTNOTES

Author contributions: Yang H contributed to the conceptualization, data curation, and writing - original draft; Qiu GP and Liu J participated in the investigation of this study; Qiu GP, Liu J, and Yang TQ took part in the writing - review & editing; Qiu GP contributed to the resources of this manuscript; Liu J was involved in the investigation of this study; Yang TQ contributed to the methodology and visualization.

Institutional review board statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Ningbo No. 2 Hospital (approval No: YJ-NBEY-KY-2024-004-01; date of approval: 2024-01-16).

Informed consent statement: The need for patient consent was waived due to the retrospective nature of the study which was approved by the Ethics Committee of Ningbo No. 2 Hospital.

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Data sharing statement: The data underlying the findings of this study are accessible upon request to the corresponding author, owing to privacy and ethical considerations that preclude their public dissemination.

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Country of origin: China

ORCID number: Tie-Quan Yang [0009-0004-3099-260X](https://orcid.org/0009-0004-3099-260X).

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