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Original Article

Drug-eluting beads transarterial chemoembolization improves tumor response and survival compared with conventional TACE in intermediate-stage hepatocellular carcinoma: a retrospective cohort study

Guiwen Shao, Jianfei Liu

Department of Interventional Therapy, The First Affiliated Hospital of Dalian Medical University, Dalian 116011, Liaoning, China

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Abstract: Transarterial chemoembolization (TACE) is standard treatment for intermediate-stage hepatocellular carcinoma (HCC), but the optimal embolization technique remains debated. This study aimed to compare effects of drug-eluting beads TACE (DEB-TACE) and conventional TACE (cTACE) on liver function and long-term survival in these patients. This retrospective investigation examined a cohort of 255 individuals diagnosed with intermediate-stage HCC, all of whom received TACE treatments at First Affiliated Hospital of Dalian Medical University between January 2019 and December 2022. Participants were categorized into cTACE group (n = 110) and DEB-TACE group (n = 145). Liver function parameters were measured at baseline, 1 week, and 1 month post-treatment. Tumor response was assessed at 1 month using mRECIST criteria. Tumor recurrence was evaluated at 3 and 6 months. Overall survival (OS) and progression-free survival (PFS) were analyzed, and adverse events were recorded. The DEB-TACE group required fewer treatment sessions (P = 0.003) and received a higher chemotherapy dose (P = 0.038). At 1 week post-treatment, DEB-TACE patients showed higher total bilirubin (TBIL, P = 0.004) and lower albumin (ALB, P = 0.012), but these differences resolved by 1 month. DEB-TACE achieved superior objective response rate (ORR, P = 0.008) and disease control rate (DCR, P = 0.019), with lower 6-month recurrence rates (P = 0.010). PFS and OS were significantly longer with DEB-TACE (P < 0.001). Multivariate analysis verified that DEB-TACE serves as an independent protective element for both PFS and OS (P < 0.001). Adverse event rates were similar between groups. DEB-TACE shows enhanced effectiveness compared to cTACE regarding tumor response, recurrence control, and long-term survival for intermediate-stage HCC, with comparable safety and only transient differences in early post-procedural liver function.

Keywords: Carcinoma, hepatocellular, chemoembolization, therapeutic, liver function tests, survival analysis, microspheres, treatment outcome

Introduction

Globally, hepatocellular carcinoma (HCC) ranks among the leading widespread types of cancer and stands out as a major source of fatalities linked to cancer [1, 2]. The incidence of HCC continues to rise globally, driven primarily by the high burden of chronic hepatitis B and C infections, as well as increasing rates of metabolic dysfunction-associated steatotic liver disease [3]. Clinical management of HCC is guided by the Barcelona Clinic Liver Cancer (BCLC) staging system, which stratifies patients into prognostic stages and links each stage to recommended treatment algorithms [4]. For patients diagnosed with intermediate-stage HCC (BCLC stage B), transarterial chemoembolization (TACE) has been established as the standard of care and first-line treatment option based on robust evidence demonstrating survival benefit [5].

Conventional TACE (cTACE) involves the intra-arterial infusion of a chemotherapeutic agent emulsified with lipiodol, followed by embolization with particulate agents. This method takes advantage of the liver's dual blood supply, with HCC primarily receiving its blood flow from the

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hepatic artery, allowing for selective tumor targeting while sparing the surrounding liver parenchyma. Despite its widespread acceptance and proven efficacy, cTACE is characterized by considerable heterogeneity in technical execution, including variability in chemotherapeutic drug selection and dosage, lipiodol emulsion preparation, and choice of embolic agents [6]. Moreover, the pharmacokinetic profile of cTACE results in rapid drug washout into the systemic circulation, potentially increasing systemic toxicity while reducing intratumoral drug concentration and retention time [7]. These limitations have prompted the development of alternative embolization technologies aimed at improving the therapeutic index of TACE [8].

Drug-eluting beads TACE (DEB-TACE) was developed to address the inherent drawbacks of conventional techniques. These microspheres are designed to load chemotherapeutic drugs through ionic exchange mechanisms and subsequently release them in a controlled and sustained manner directly within the tumor vasculature [9]. This technology offers several theoretical advantages: it ensures more predictable and standardized drug delivery, achieves higher and more sustained intratumoral drug concentrations, and minimizes systemic drug exposure and associated adverse effects [10-12]. Furthermore, DEB-TACE combines the functions of drug delivery and embolization into a single device, potentially simplifying the procedure and improving consistency across operators and institutions [13].

The introduction of DEB-TACE into clinical practice has generated substantial interest in determining whether its theoretical benefits translate into meaningful improvements in patient outcomes. Previous comparative studies have yielded conflicting results regarding tumor response rates and survival benefits, with some investigations demonstrating superiority of DEB-TACE and others showing comparable efficacy between the two techniques. Additionally, there are worries about the possible rise in biliary toxicity and ischemic complications with DEB-TACE, particularly in patients with underlying liver dysfunction. Importantly, the impact of these two TACE modalities on longitudinal liver function changes remains incompletely characterized, despite the critical importance of preserving hepatic reserve in a population already at risk for liver decompensation. Given these unresolved questions and the need for further evidence to guide clinical decision-making, this study was devised to evaluate the impact of DEB-TACE versus cTACE on liver function indicators and long-term survival rates in intermediate-stage HCC patients.

Methods

Subjects selection

Patients: This study conducted a retrospective analysis of 255 patients with intermediate-stage hepatocellular carcinoma (HCC) who underwent transarterial chemoembolization (TACE) at the First Affiliated Hospital of Dalian Medical University from January 2019 to December 2022. According to the treatment modality received, patients receiving conventional TACE were categorized into cTACE group (n = 110), while patients receiving drug-eluting beads TACE were classified into the DEB-TACE group (n = 145). Patient inclusion criteria included: compliance with European Association for the Study of the Liver (EASL) diagnostic criteria for HCC [14]; BCLC stage B (intermediate stage); Child-Pugh class A or B; ECOG performance status score 0-1; age ≥ 18 years; first-time recipients of TACE treatment; complete clinical and follow-up data. Exclusion criteria included the following situations: previous receipt of TACE, ablation, surgical resection, or systemic therapy; presence of main portal vein tumor thrombus or extrahepatic metastasis; diffuse HCC or tumor burden > 50%; Child-Pugh class C or severe coagulation dysfunction; coexistence of other malignant tumors; severe infection or organ failure; pregnancy or lactation; allergy to contrast agents or chemotherapeutic drugs.

Ethical statement: This study followed the 1964 Helsinki Declaration and its subsequent amendments, and it received approval from the Ethics Committee of the First Affiliated Hospital of Dalian Medical University. Given that this study involved a retrospective analysis of anonymized medical records, the requirement for informed consent was waived. To ensure privacy, all patient data were anonymized, and stringent confidentiality protocols were enforced throughout the study.

Treatment measures

cTACE group: Employing the Seldinger technique for femoral artery puncture, celiac trunk and superior mesenteric artery angiography were conducted following catheter placement. Following identification of tumor-supplying arteries, superselective catheterization was conducted into the tumor-supplying arteries. The chemotherapeutic drug epirubicin (Pfizer Pharmaceutical Co., Ltd., H20000496, Specification: 10 mg/vial) 50 mg and lipiodol (Yantai Luyin Pharmaceutical Co., Ltd., H37022299, Specification: 10 mL/vial) were fully emulsified in a 1:1 ratio and slowly injected, with specific dosages adjusted according to tumor size and blood supply conditions (epirubicin 40-60 mg, lipiodol 5-20 mL). After injection completion, if necessary, gelatin sponge particles (Hangzhou Alicon Pharmaceutical Technology Co., Ltd., Specification: 350-560 μm) were used to enhance embolization until tumor-supplying artery blood flow stagnated.

DEB-TACE group: Using the same puncture and catheterization techniques, after superselective catheterization into tumor-supplying arteries, CalliSpheres® drug-eluting beads (Jiangsu Hengrui Pharmaceutical Co., Ltd., Specification: 100-300 μm) were used for embolization. The beads were loaded with epirubicin (same as cTACE group); the loading method involved dissolving epirubicin in an appropriate amount of water for injection, thoroughly mixing with the beads, and allowing static settlement for 30 minutes for complete drug adsorption. According to tumor size, number, and blood supply conditions, the loading dose of epirubicin was 40-70 mg. Bead particle size and quantity were selected based on tumor size, number, and blood supply conditions, and slowly injected into tumor-supplying arteries, with the embolization endpoint being disappearance of tumor staining and stagnation of supplying artery blood flow.

The different embolization endpoints reflect the distinct technical characteristics of the two procedures. For cTACE, lipiodol is used as the primary embolic agent, and gelatin sponge particles are added only when necessary to achieve blood flow stasis. For DEB-TACE, the microspheres themselves provide both drug delivery and embolic effects, and the endpoint of complete tumor staining disappearance is a standardized clinical criterion for this technique. A unified endpoint was not adopted because the mechanisms of embolization differ substantially between the two modalities. However, both endpoints were consistently applied within each group by the same interventional team, ensuring internal validity.

For the cTACE group, chemotherapy drug dosage refers to the dose of epirubicin injected directly as part of the lipiodol emulsion. For the DEB-TACE group, it refers to the loading dose of epirubicin absorbed onto the CalliSpheres microspheres. Due to different pharmacokinetic profiles (sustained release from beads vs. rapid washout with cTACE), the loaded/injected doses are not directly equivalent in terms of intratumoral drug exposure. The comparison presented here reflects clinical practice dosing based on tumor burden and does not imply bioequivalence.

Both group procedures were completed by the same interventional treatment team following standardized processes, with routine intraoperative cardiac monitoring and administration of antiemetic and analgesic drugs. Postoperatively, all patients received symptomatic and supportive treatments including liver protection (such as magnesium isoglycyrrhizinate, adenosylmethionine), antiemetics, and analgesics. Based on enhanced CT/MRI evaluation results at 6-8 weeks post-surgery, if residual viable lesions existed and liver function permitted (Child-Pugh score without deterioration or with improvement), repeat treatment could be performed, with the repeat treatment regimen consistent with the original plan.

Data collection and measurement methods

The data collection process in this study strictly followed a predefined protocol to ensure accuracy and reliability. All patient data originated from electronic medical record system of hospital, with collected content including demographic information (age, sex, body mass index), clinical characteristics (cirrhosis status, etiology, Child-Pugh class, ECOG PS score), tumor characteristics (maximum tumor diameter, number of tumors > 3, bilobar involvement, BCLC substage, venous invasion), treatment parameters (number of treatments, chemotherapeutic drug dosage, embolic agent dosage, technical success rate, hospitalization days), laboratory indicators (alanine aminotransferase, aspartate aminotransferase, total bilirubin, albumin, prothrombin time, collected at baseline, 1 week post-surgery, and 1 month post-surgery respectively), and follow-up data (tumor response, recurrence status, survival status, adverse events). All data underwent double-checking by two individuals to ensure accuracy.

Outcomes

Primary outcome measure: (1) Liver Function Index Detection Methods: Fasting elbow venous blood samples (5 mL) were collected from patients prior to surgery, one week post-surgery, and one month post-surgery, injected into vacuum blood collection tubes containing separation gel, allowed to stand for 30 minutes, and subsequently centrifuged at 3000 r/min for 10 minutes (LDZ5-2 low-speed automatic balanced centrifuge, Beijing Jingli Centrifuge Co., Ltd., China) to separate serum. Testing was performed using a Fujifilm DRI-CHEM NX500i automatic dry chemistry biochemical analyzer (Fujifilm Corporation, Japan) with matching reagent slides. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were detected though enzymatic rate method; total bilirubin (TBIL) was detected using diazo method; albumin (ALB) was detected using bromocresol green method; prothrombin time (PT) was measured using the coagulation method on a CS-5100 automatic coagulation analyzer (Sysmex Corporation, Japan), using matching prothrombin time reagent (Dade® Innovin®, Siemens Healthcare, Germany). All tests were strictly performed in accordance with instrument standard operating protocols, including daily quality control calibration to ensure accurate and reliable results.

(2) Long-term survival indicators included overall survival (OS) and progression-free survival (PFS). OS was characterized as the duration from the initial treatment to death from any cause, while PFS was characterized as the interval from first treatment to first recorded disease progression or death from any cause. Follow-up ended in December 2025. The median follow-up time was 46.5 months (range: 3.2 to 84.0 months). Survival data were obtained through outpatient follow-up records and telephone follow-up.

Secondary outcome measure: (1) Tumor response assessment: One month after surgery, patients underwent upper abdominal enhanced CT or MRI scans. Two radiologists assessed tumor response utilizing modified Response Evaluation Criteria in Solid Tumors (mRECIST), each with more than a decade of experience. Enhanced CT used SOMATOM Definition Flash dual-source CT (Siemens Healthcare, Germany), with scanning parameters: tube voltage 120 kV, tube current 200-250 mAs, slice thickness 5 mm, contrast agent iohexol (350 mgI/mL, GE Healthcare, China), injection rate 3-4 mL/s, arterial phase scan delay 20-25 seconds, portal venous phase delay 60-70 seconds. Enhanced MRI used MAGNETOM Skyra 3.0T superconducting magnetic resonance (Siemens Healthcare, Germany), with scanning sequences including T1WI, T2WI, diffusion-weighted imaging (DWI), and dynamic contrast-enhanced scanning, contrast agent gadoxetic acid disodium (Primovist®, Bayer Pharma, Germany), injection dose 0.1 mL/kg. According to mRECIST criteria [15], complete response (CR) was characterized by disappearance of arterial phase enhancement in all target lesions. Partial response (PR) was determined when there was at least a 30% decrease in total diameter of target lesions (measured during arterial phase enhancement). Stable disease (SD) was noted if changes in lesion size fell between PR and progressive disease (PD). PD was characterized by a 20% or greater rise in the total diameter of target lesions (during arterial phase enhancement) or the emergence of new lesions. Objective response rate (ORR) represents the total of CR and PR, whereas disease control rate (DCR) reflects the total of CR, PR, and SD. These metrics were then determined.

(2) Tumor recurrence assessment: At 3 and 6 months after surgery, the same imaging methods were used to assess local recurrence (enhancing foci appearing in the original lesion area), new lesions (new lesions appearing in other parts of the liver), and overall recurrence.

(3) Adverse event assessment: Adverse events were recorded and classified in accordance with Common Terminology Criteria for Adverse

Table 1. Sociodemographic and clinical characteristics of the subjects

Parameters	cTACE Group (n = 110)	DEB-TACE Group (n = 145)	t/χ^2	P
Age (years)	64.42 ± 9.34	63.56 ± 8.82	0.753	0.452
Gender (male/female) (n, %)	83 (75.45%)	113 (77.93%)	0.216	0.642
BMI (kg/m^2)	23.03 ± 3.26	22.76 ± 3.15	0.673	0.502
Cirrhosis (n, %)	92 (83.63%)	124 (85.52%)	0.171	0.679
Etiology (n, %)			2.590	0.459
HBV	67 (60.91%)	91 (62.76%)		
HCV	17 (15.45%)	30 (20.69%)		
Alcohol	7 (6.36%)	6 (4.14%)		
Other and mixed	19 (17.28%)	18 (12.41%)		
Child-Pugh class (A/B) (n, %)	88 (80.00%)	121 (83.45%)	0.503	0.478
ECOG PS (0/1) (n, %)	79 (71.81%)	108 (74.48%)	0.227	0.634

BMI: Body Mass Index; HBV: Hepatitis B Virus; HCV: Hepatitis C Virus; ECOG PS: Eastern Cooperative Oncology Group Performance Status.

Events (CTCAE version 5.0) [16]. Common adverse events (grades 1-2) included abdominal pain, fever (> 38°C), nausea/vomiting, and transient liver injury; serious adverse events (grades 3-4) included severe liver failure, biliary infection/abscess, hepatic artery injury, and non-target embolization. All adverse events were independently assessed by two clinicians, with consensus reached through discussion in case of disagreement.

Statistical analysis

Analyzing data through SPSS 29.0 (IBM Corp., USA). Categorical data were reported as (n, %) and compared across groups by χ^2 test. Continuous variables were first evaluated for normality via Shapiro-Wilk test. Data that followed a normal distribution were shown as mean ± standard deviation (Mean ± SD), and group comparisons were performed utilizing independent samples t-test. For longitudinal liver function parameters, a repeated measures analysis of variance (ANOVA) was performed with time as the within-subject factor and treatment group as the between-subject factor. The time × group interaction was examined. Post-hoc comparisons at each time point were conducted using Bonferroni correction. Sphericity was assessed with Mauchly's test and Greenhouse-Geisser correction applied as needed. Other analyses were performed as described previously. Survival analysis employed Kaplan-Meier method to plot survival curves, with intergroup comparison using the log-rank test. Variables with a univariate *P* value < 0.10 or those considered clinically relevant based on prior literature (including treatment modality, tumor diameter, tumor number, Child-Pugh class, and venous invasion) were entered into the multivariate Cox regression model using a forward stepwise approach. All statistical tests were two-tailed, with a *P*-value less than 0.05 deemed significant.

Results

Baseline data of HCC subjects undergoing TACE

This study encompassed 255 patients with intermediate-stage HCC, where 110 patients underwent conventional TACE and 145 patients received DEB-TACE. Baseline sociodemographic and clinical characteristics were well-balanced between two groups. No notably statistical differences were observed in age, gender distribution, BMI, presence of cirrhosis, etiology of liver disease, Child-Pugh class, or ECOG performance status (all P > 0.05, **Table 1**).

Similarly, the tumor characteristics were similar between groups. No notable variations were observed in maximum tumor diameter, the proportion of patients with more than three tumors, bilobar involvement, BCLC substage, or the presence of venous invasion (all P > 0.05, **Table 2**).

Treatment details

Table 3 shows the treatment details for both groups. DEB-TACE group underwent notably

Table 2. Tumor characteristics of the subjects

Parameters	cTACE Group (n = 110)	DEB-TACE Group (n = 145)	t/χ^2	P
Maximum tumor diameter (cm)	5.22 ± 1.73	5.01 ± 1.62	1.003	0.317
Number of tumors > 3 (n, %)	38 (34.55%)	45 (31.03%)	0.351	0.553
Bilobar involvement (n, %)	42 (38.18%)	50 (34.48%)	0.371	0.542
BCLC substage (B2/B3) (n, %)	72 (65.45%)	90 (62.07%)	0.309	0.578
Venous invasion (n, %)	25 (22.7%)	28 (19.3%)	0.444	0.505

BCLC: Barcelona Clinic Liver Cancer.

Table 3. Comparison of treatment details of the subjects

Parameters	cTACE Group (n = 110)	DEB-TACE Group (n = 145)	t	P
Number of treatments (times)	2.32 ± 0.60	2.11 ± 0.52	2.968	0.003
Chemotherapy drug dosage (mg)	48.53 ± 12.31	52.12 ± 14.55	2.085	0.038
Embolic agent dosage (mL)	8.22 ± 2.51	7.72 ± 2.24	1.664	0.097
Technical success rate (%)	98.23 ± 4.15	98.69 ± 3.84	0.909	0.364
Hospitalization days (days)	5.44 ± 1.74	5.68 ± 1.85	1.051	0.294

Table 4. Repeated measures ANOVA for liver function parameters

Parameters	Effect	F	P
ALT	Time	485.23	< 0.001
	Group	1.34	0.248
	Time × Group	0.85	0.432
AST	Time	398.72	< 0.001
	Group	1.12	0.291
	Time × Group	1.12	0.329
TBIL	Time	67.23	< 0.001
	Group	3.71	0.055
	Time × Group	6.82	0.002
ALB	Time	89.45	< 0.001
	Group	1.38	0.241
	Time × Group	4.95	0.008
PT	Time	24.67	< 0.001
	Group	0.73	0.394
	Time × Group	0.63	0.537

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; TBIL: Total bilirubin; ALB: Albumin; PT: Prothrombin time. ns: no significant difference.

fewer treatment sessions than cTACE group (2.11 ± 0.52 vs. 2.32 ± 0.60, P = 0.003). Furthermore, the chemotherapy drug dosage administered was markedly greater in DEB-TACE group (52.12 ± 14.55 mg) than in cTACE group (48.53 ± 12.31 mg, P = 0.038). No conspicuous variations were noted between groups with respect to embolic agent dosage, technical success rate, or length of hospital stay (all P > 0.05).

Changes in liver function

Repeated measures ANOVA showed significant time × group interactions for TBIL (F = 6.82, P = 0.002) and ALB (F = 4.95, P = 0.008, **Table 4**). Post-hoc pairwise comparisons with Bonferroni correction revealed that at one week post-treatment, the DEB-TACE group had significantly higher TBIL (32.16 ± 10.52 vs. 28.52 ± 9.34 μmol/L, adjusted P = 0.004) and lower ALB (33.01 ± 4.14 vs. 34.29 ± 3.82 g/L, adjusted P = 0.012) than the cTACE group (**Figure 1**). No significant differences were observed at baseline or one month for any parameter (all adjusted P > 0.05). For ALT, AST, and PT, the time × group interactions were not significant (all P > 0.05).

Treatment response

Tumor response assessment one month after the first TACE session is detailed in **Table 5**. The DEB-TACE group demonstrated a significantly better ORR compared to the cTACE group (68.97% vs. 52.73%, P = 0.008). The DCR was also significantly higher in the DEB-TACE group (89.66% vs. 79.09%, P = 0.019).

Tumor recurrence status

Analysis of tumor recurrence at 3 and 6 months post-treatment is shown in **Table 6.** At both time points, the DEB-TACE group exhibited significantly lower rates of local recur-

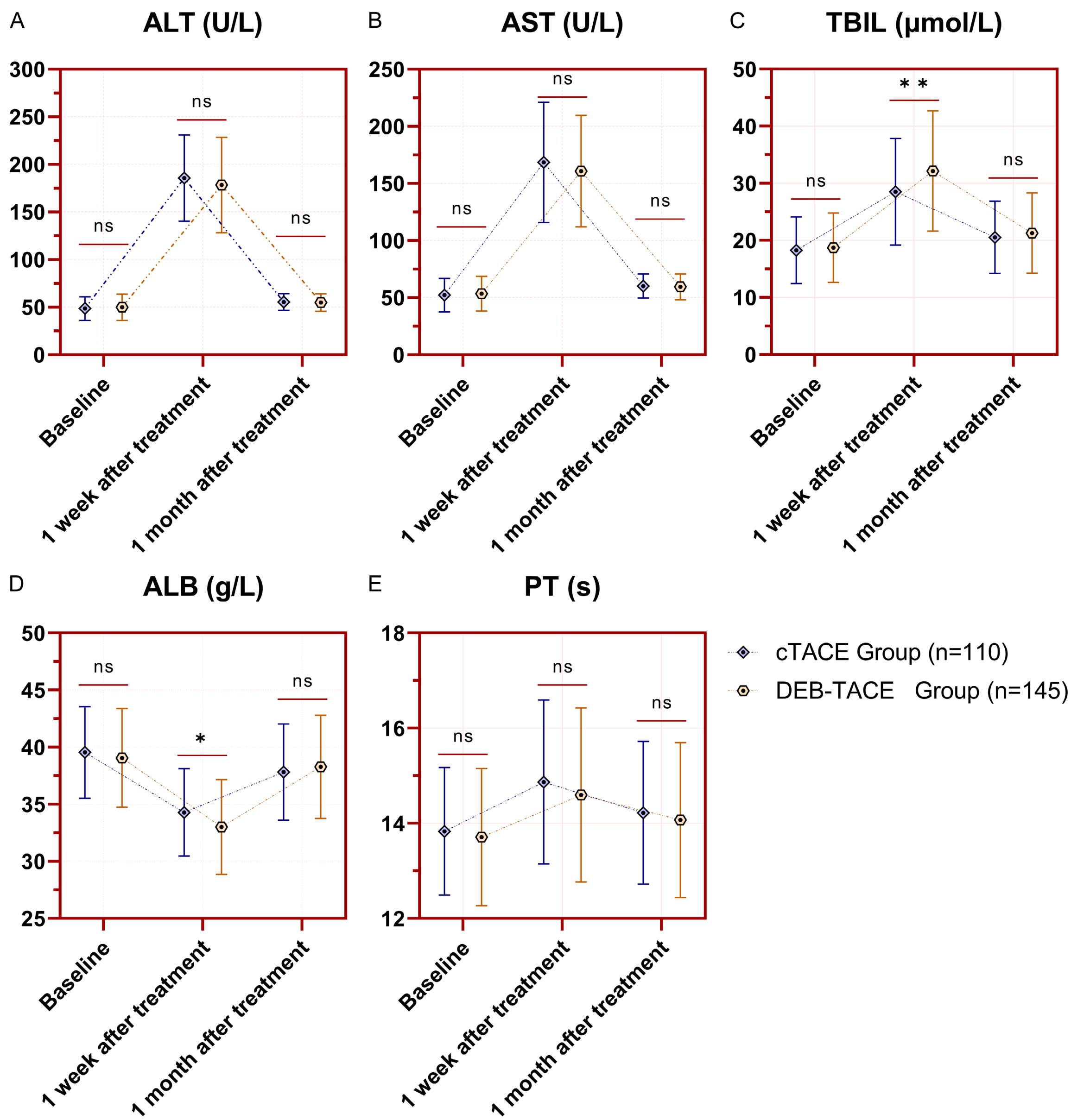

Figure 1. Comparison of Changes in Liver Function of the Subjects Before and After Treatment. A: ALT (U/L); B: AST (U/L); C: TBIL (μmol/L); D: ALB (g/L); E: PT (s). ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; TBIL: Total bilirubin; ALB: Albumin; PT: Prothrombin time. ns: no significant difference; *: P < 0.05; **: P < 0.01.

Table 5. Comparison of treatment response of the subjects 1 month after the first treatment (n, %)

Parameters	cTACE Group (n = 110)	DEB-TACE Group (n = 145)	X^2	P
CR	16 (14.55%)	37 (25.52%)		
PR	42 (38.18%)	63 (43.45%)		
SD	29 (26.36%)	30 (20.69%)		
PD	23 (20.91%)	15 (10.34%)		
ORR (CR+PR)	58 (52.73%)	100 (68.97%)	6.998	0.008
DCR (CR+PR+SD)	87 (79.09%)	130 (89.66%)	5.505	0.019

CR: Complete response; PR: Partial response; SD: Stable disease; PD: Progressive disease; ORR: Overall response rate; DCR: Disease control rate.

rence compared to the cTACE group (3 months: 8.97% vs. 22.73%, P = 0.002; 6 months: 20.7% vs. 38.18%, P = 0.002). Incidence of new lesions was also decreased in DEB-TACE group, but differences did not reach statistical significance (3 months: 6.90% vs. 12.73%, P = 0.114; 6 months: 11.69% vs. 19.09%, P = 0.070). Consequently, overall recurrence rate was significantly lower in DEB-TACE group at both 3 months (15.86% vs. 28.18%, P = 0.017)

Table 6. Comparison of tumor recurrence status of the subjects (n, %)

Parameters		cTACE Group (n = 110)	DEB-TACE Group (n = 145)	t	P
3 months after treatment	Local recurrence	25 (22.73%)	13 (8.97%)	9.341	0.002
	New lesions	14 (12.73%)	10 (6.90%)	2.494	0.114
	Overall recurrence	31 (28.18%)	23 (15.86%)	5.687	0.017
6 months after treatment	Local recurrence	42 (38.18%)	30 (20.7%)	9.445	0.002
	New lesions	21 (19.09%)	16 (11.69%)	3.273	0.070
	Overall recurrence	44 (40.00%)	36 (24.83%)	6.688	0.010

and 6 months (24.83% vs. 40.00%, P = 0.010).

Survival outcome analysis

Survival outcomes are summarized in **Figure 2**. Patients treated with DEB-TACE had a notably longer PFS than those treated with cTACE (13.23 ± 3.54 months vs. 9.52 ± 2.81 months, P < 0.001). Furthermore, the DEB-TACE group also demonstrated a significantly superior OS (28.17 ± 5.63 months vs. 20.55 ± 4.14 months, P < 0.001).

Multivariate analysis of factors associated with survival

Multivariate Cox regression analysis was performed to identify independent predictors of OS and PFS (**Table 7**). After taking into account potential confounders including tumor diameter, number of tumors, Child-Pugh class, and venous invasion, DEB-TACE treatment continued to be an independent protective factor for both PFS (HR = 0.578, P < 0.001) and OS (HR = 0.519, P < 0.001). Tumor diameter > 5 cm was independently linked to poorer PFS (HR = 1.543, P = 0.004) and OS (HR = 1.672, P = 0.001). Venous invasion also emerged as a notable indicator of poorer PFS (HR = 1.723, P = 0.002) and OS (HR = 1.893, P < 0.001). Child-Pugh class B showed a bor-

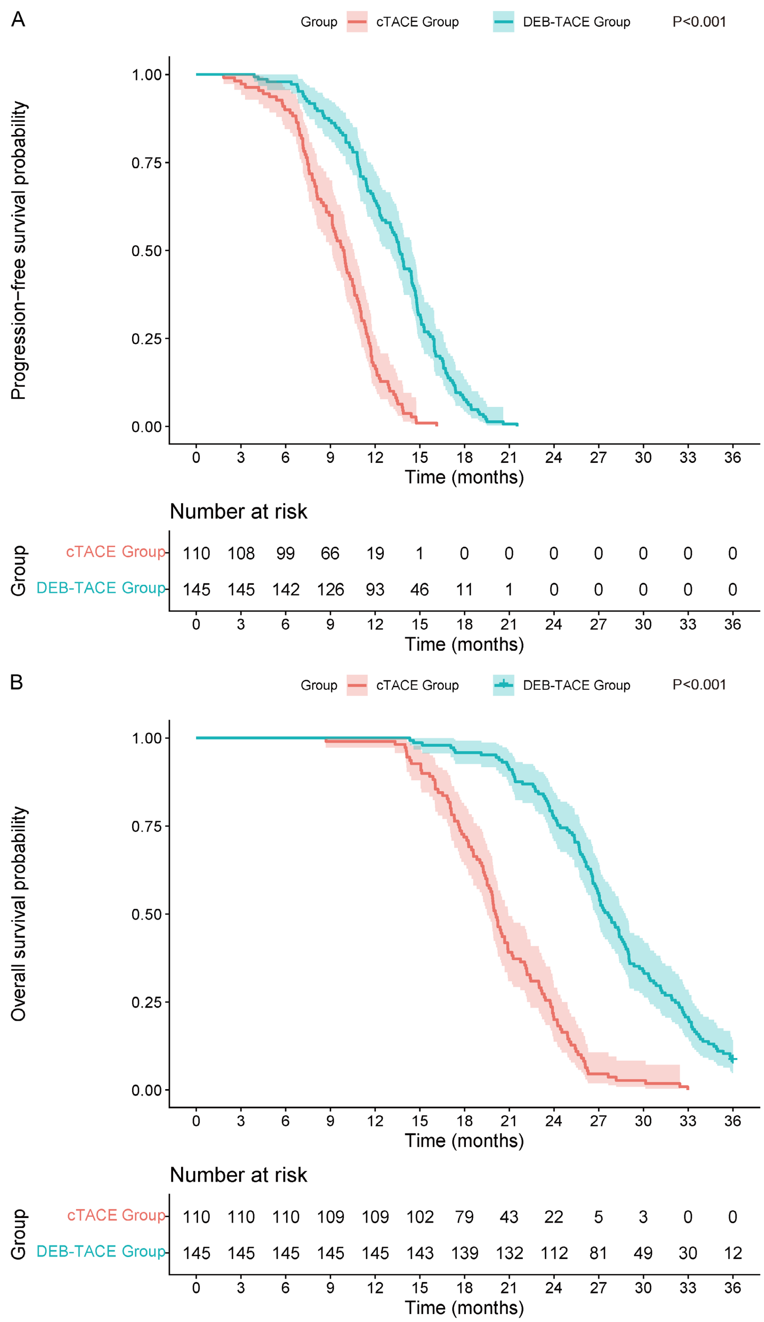

Figure 2. Kaplan-Meier Curve of OS Time and PFS Time by Treatments. A: PFS (months); B: OS (months). PFS: Progression-Free Survival; OS: Overall Survival.

Table 7. Multivariate cox regression analysis of factors associated with survival

Variables	PFS		OS	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
DEB-TACE (vs. cTACE)	0.578 (0.426-0.785)	< 0.001	0.519 (0.377-0.714)	< 0.001
Tumor diameter > 5 cm	1.543 (1.148-2.074)	0.004	1.672 (1.228-2.277)	0.001
Number of tumors > 3	1.324 (0.976-1.796)	0.069	1.287 (0.936-1.769)	0.118
Child-Pugh B (vs. A)	1.415 (0.987-2.028)	0.058	1.458 (1.008-2.109)	0.045
Venous invasion	1.723 (1.225-2.422)	0.002	1.893 (1.338-2.679)	< 0.001

HR: hazard ratio; CI: confidence interval; PFS: Progression-Free Survival; OS: Overall Survival.

Table 8. Comparison of common postoperative adverse events (CTCAE grades 1-2) of the subjects (n, %)

Parameters	cTACE Group (n = 110)	DEB-TACE Group (n = 145)	χ^2	P
Abdominal pain	60 (54.55%)	85 (58.62%)	0.423	0.515
Fever (> 38°C)	45 (40.91%)	68 (46.90%)	0.909	0.340
Nausea/Vomiting	32 (29.09%)	38 (26.21%)	0.261	0.609
Transient liver injury	68 (61.82%)	78 (53.79%)	1.646	0.200

CTCAE: Common Terminology Criteria for Adverse Events.

Table 9. Comparison of Serious Adverse Event (CTCAE Level 3-4) of the Subjects (n, %)

Parameters	cTACE Group (n = 110)	DEB-TACE Group (n = 145)	χ^2	P
Severe liver failure	3 (2.73%)	2 (1.38%)	0.098	0.754
Biliary infection/Abscess	4 (3.64%)	3 (2.07%)	0.138	0.710
Hepatic artery injury	1 (0.91%)	2 (1.38%)	0.058	0.809
Non-target embolism	2 (1.82%)	1 (0.69%)	0.058	0.809

CTCAE: Common Terminology Criteria for Adverse Events.

derline notable connection to worse OS (HR = 1.458, P = 0.045), but its effect on PFS did not achieve statistical significance (HR = 1.415, P = 0.058). Number of tumors > 3 was not an independent predictor for either PFS or OS in this multivariate model (P > 0.05).

Safety assessment

The safety profiles of both treatments are compared in **Tables 8** and **9**. Regarding common adverse events (CTCAE grades 1-2), no notably statistical distinctions were noted between cTACE and DEB-TACE groups in incidence of abdominal pain, fever, nausea/vomiting, or transient liver injury (all P > 0.05, **Table 8**). Similarly, incidence of serious adverse events (CTCAE grades 3-4), including severe liver failure, biliary infection/abscess, hepatic artery injury, and non-target embolism, was low and similar between two groups, with notably statistical distinctions were noted (all P > 0.05, as shown in **Table 9**).

Discussion

This retrospective comparative analysis demonstrated that DEB-TACE provides several benefits relative to cTACE in the management of intermediate-stage HCC, including reduced treatment frequency, improved tumor response, lower recurrence rates, and superior long-term survival outcomes, while maintaining a comparable safety profile with only transient differences in early post-procedural liver function.

The observation that patients in the DEB-TACE group required fewer treatment sessions compared to those receiving cTACE aligns with the fundamental pharmacokinetic differences between these two techniques [17]. DEB-TACE enables sustained and controlled drug release directly within the tumor vasculature, potentially achieving more complete tumor necrosis in a single procedure [18, 19]. These results align with prior studies demonstrating that DEB-TACE patients underwent fewer treatment sessions compared to cTACE recipients [20]. The higher chemotherapy dosage administered in the DEB-TACE group, despite fewer procedures, reflects the ability of drug-eluting beads to deliver concentrated chemotherapeutic agents directly to the tumor bed without corresponding increases in systemic toxicity, a theoretical advantage that has been well documented in the literature [21].

Regarding liver function changes, both groups experienced expected post-procedural elevations in transaminases and bilirubin with corresponding decreases in albumin, reflecting the ischemic and cytotoxic insult to hepatic parenchyma inherent to TACE procedures [22]. However, the DEB-TACE group exhibited higher total bilirubin levels and lower albumin levels at one week post-treatment compared to the cTACE group. This transient exaggeration of liver function disturbance may be attributable to the more complete and distal embolization achieved with calibrated microspheres, potentially affecting a greater volume of peritumoral liver parenchyma [23]. Additionally, the sustained drug release from beads may prolong the period of hepatocyte stress. Similar findings have been reported by Xiang and colleagues, who observed greater decreases in albumin from baseline to one week in DEB-TACE patients compared to cTACE patients [24]. Importantly, these differences resolved by one month, indicating that the initial hepatic insult is reversible and does not translate into persistent liver function impairment [25]. This pattern suggests that DEB-TACE does not carry an elevated risk of long-term hepatotoxicity, a finding that contrasts with some previous concerns regarding potential biliary toxicity with bead-based embolization.

The superior tumor response rates observed with DEB-TACE, including higher objective response and disease control rates at one month, corroborate the enhanced pharmacokinetic profile of drug-eluting beads. The ability of microspheres to maintain high intratumoral drug concentrations over an extended period likely contributes to more effective tumor killing [13]. This finding aligns with multiple previous investigations that have demonstrated improved response rates with DEB-TACE compared to conventional techniques [26, 27]. A recent comparative analysis similarly reported higher disease control rates with DEB-TACE, particularly in patients receiving treatment as bridging to transplantation [28]. The improved response rates translated directly into reduced tumor recurrence at both three and six months, with DEB-TACE patients showing lower rates of local recurrence, new lesion development, and overall recurrence. This pattern likely reflects more complete initial devascularization and sterilization of the tumor microenvironment, reducing the substrate for subsequent tumor regrowth and intrahepatic spread [29].

The most clinically meaningful findings of this study relate to the long-term survival outcomes, with DEB-TACE patients experiencing prolonged progression-free survival and overall survival than cTACE recipients [30]. These survival benefits represent the cumulative effect of improved initial response, reduced recurrence, and preserved liver function over time. The magnitude of survival improvement observed in this study exceeds that reported in some earlier comparative investigations, which may reflect refinements in patient selection, technical execution, or the specific characteristics of the CalliSpheres beads used in this analysis [23]. While some previous studies have failed to demonstrate survival differences between these techniques, others have shown survival benefits favoring DEB-TACE, particularly in specific patient subgroups [31, 32]. The independent prognostic value of DEB-TACE was further confirmed by multivariate Cox regression analysis, which demonstrated that DEB-TACE remained a protective effect on both PFS and OS after adjusting for potential confounders including tumor diameter, tumor number, Child-Pugh class, and venous invasion. Regarding baseline liver function, Child-Pugh class B showed a borderline association with worse PFS and a significant association with worse OS. Although the PFS result did not reach statistical significance, the consistent trend suggests that baseline liver function reserve may have a clinically meaningful impact on prognosis, particularly in the context of TACE treatment. This finding strengthens the evidence that the survival benefit associated with DEB-TACE is not merely attributable to differences in baseline characteristics but reflects a true treatment effect. The present findings contribute to the growing body of evidence supporting DEB-TACE as a preferred embolization strategy for appropriate candidates with intermediate-stage HCC.

The comparable safety profile between the two techniques, with similar rates of common adverse events and serious complications, reinforces the clinical utility of DEB-TACE [22]. Despite theoretical concerns regarding increased biliary toxicity with bead-based embolization, the present analysis did not identify elevated risks of biliary complications or severe liver failure in the DEB-TACE group. The rates of post-embolization syndrome symptoms, including abdominal pain, fever, and nausea, were similar between groups, consistent with previous reports demonstrating acceptable safety profiles for DEB-TACE [11]. The absence of increased serious adverse events suggests that DEB-TACE can be performed safely across a broad spectrum of intermediate-stage HCC patients.

This study is subject to several limitations that need to be recognized. Although the baseline characteristics were comparable across the groups, the study's design, being retrospective and limited to a single center, could lead to potential selection bias. Study period spanned several years, during which refinements in imaging technology, supportive care, and technical expertise may have influenced outcomes. The use of a single chemotherapeutic agent (epirubicin) and specific bead type (CalliSpheres) limits generalizability to other drug-bead combinations. Furthermore, the comparison of chemotherapeutic doses between the two groups should be interpreted with caution, as the loaded dose in DEB-TACE and the injected dose in cTACE are not pharmacokinetically equivalent. Future studies incorporating intratumoral drug concentration measurements would strengthen comparative effectiveness assessments. Additionally, the exclusion of patients with more advanced liver dysfunction or tumor burden restricts applicability to the broader HCC population encountered in clinical practice. Future prospective randomized controlled trials employing standardized protocols and extended follow-up periods are necessary to confirm these findings and identify patient subgroups most likely to derive differential benefit from each technique. Investigations incorporating life's quality assessments and economic efficiency analyses would further provide additional guidance for clinical decision-making. Despite these limitations, the present study provides meaningful evidence supporting DEB-TACE as an effective and safe treatment modality for intermediate-stage HCC, offering advantages in tumor control and long-term survival than conventional techniques.

Conclusion

In conclusion, this retrospective comparative analysis demonstrates that DEB-TACE provides meaningful advantages over cTACE for intermediate-stage HCC patients. DEB-TACE was associated with improved tumor response rates, reduced tumor recurrence at early follow-up time points, and superior progression-free and overall survival outcomes compared to conventional techniques. These clinical benefits were achieved while maintaining a comparable safety profile, with only transient differences in early post-procedural liver function parameters that resolved within one month. The reduced number of treatment sessions required in the DEB-TACE group suggests potential healthcare utilization benefits in addition to the clinical efficacy advantages. These results highlight DEB-TACE as a favored embolization technique for appropriately selected intermediate-stage HCC patients, contributing to accumulating evidence favoring drug-eluting bead technology over conventional lipiodol-based approaches. The independent protective effect of DEB-TACE confirmed by multivariate analysis further strengthens the robustness of these conclusions. Prospective randomized trials with standardized protocols and longer follow-up remain warranted to further refine patient selection criteria and confirm the durability of the survival benefits observed in this study.

Disclosure of conflict of interest

None.

Address correspondence to: Jianfei Liu, Department of Interventional Therapy, The First Affiliated Hospital of Dalian Medical University, No. 222 Zhongshan Road, Xigang District, Dalian 116011, Liaoning, China. E-mail: dyfyljf200201@126.com

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