Original Article

# Transarterial chemoembolization using drug-eluting beads versus lipiodol in the treatment of unresectable hepatocellular carcinoma: propensity score matching

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**Background:** Since the introduction of drug-eluting beads (DEB), the result comparing transarterial chemoembolization (TACE) using lipiodol, also called conventional transarterial chemoembolization (c-TACE), and DEB-TACE shows considerable controversy. The objective of this study was to compare the safety and efficacy of c-TACE and DEB-TACE to treat unresectable hepatocellular carcinoma (uHCC).

**Methods:** This retrospective study used propensity score matching (PSM) analysis to analyze clinical data from 113 cases of primary hepatocellular carcinoma (HCC) treated at our hospital from September 2016 to July 2021. The safety and efficacy of the two treatment modalities were analyzed after 1:1 matching. The primary endpoint was progression-free survival (PFS); the secondary endpoints included overall survival (OS), disease control rates (DCRs), and objective response rates (ORRs) at 1, 3, 6, and 12 months, and postoperative complications.

**Results:** Twenty-nine patients underwent DEB-TACE and 84 received c-TACE; 28 pairs of patients were eventually matched. After matching, baseline characteristics between groups were comparable. The median PFS of the DEB-TACE group was 10 months compared to 6 months in the c-TACE group (P=0.002). The median OS was 23 months in the DEB-TACE group *vs.* 14 months in the c-TACE group, but the difference was not statistically significant (P=0.265). The ORR at 1, 3, 6, and 12 months in the DEB-TACE group (69%, 78%, 60%, and 52%) were significantly higher than those in the c-TACE group (39%, 39%, 26%, and 8%) (P<0.05). The DCR at postoperative 3 months was significantly higher in the DEB-TACE group (95%) (P<0.05). There was one case of postoperative liver abscess in the DEB-TACE group, and the patient recovered well after drainage. No serious complications occurred.

**Conclusions:** Compared to c-TACE, DEB-TACE prolonged PFS and exhibited better short-term ORR with a similar level of safety. However, there was no significant advantage in terms of OS.

**Keywords:** Unresectable hepatocellular carcinoma (uHCC); drug-eluting beads (DEB); transarterial chemoembolization (TACE); propensity score matching (PSM)

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## Introduction

Despite advances in targeted therapy and immunotherapy, transarterial chemoembolization (TACE) remains the primary treatment approach for intermediate to advanced-stage unresectable hepatocellular carcinoma (uHCC) (1,2). There are two TACE techniques: conventional TACE (c-TACE), which uses iodized oil as the embolic agent and drug carrier, and drug-eluting beads-TACE (DEB-TACE), based on novel drug-eluting microspheres. Since the introduction of drug-eluting microspheres, comparing these two treatment methods has been a topic of interest (3-5).

c-TACE is criticized for its widespread heterogeneity, characterized by variations in drug types, dosages, strictness of microcatheter super-selection to target vessels, and the use of embolic materials across different regions and hospitals. This heterogeneity has led to inconsistent evaluations of c-TACE's efficacy in treating primary hepatocellular carcinoma (HCC), subsequently affecting the role of interventional therapy in HCC. The main advantages of DEB-TACE over c-TACE include large drug-carrying doses, long sustained release time and low peripheral drug dose (6). Consequently, the application of DEB-TACE has grown in recent years. However, there is considerable controversy concerning whether DEB-TACE is superior to c-TACE in treating primary HCC, particularly in terms of extending the overall survival (OS) of patients.

The best approach to verify the efficacy of these treatment methods is via randomized controlled trials (RCTs). Nevertheless, in the real world, RCTs are exceptionally challenging to perform due to factors like the high cost of drug-eluting microspheres, the comprehensive nature of HCC TACE treatment (often combined with systemic anti-tumor therapy), and challenges in obtaining patient informed consent. Moreover, case-control studies are prone to imbalances in confounding factors between groups and selection biases, which can lead to biased results and lower levels of evidence.

Therefore, this study aimed to employ propensity score matching (PSM) to compare the safety and efficacy of DEB-TACE and c-TACE in the treatment of unresectable primary HCC. We present this article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-369/rc).

### Highlight box

**Key findings**

- Drug-eluting beads-transarterial chemoembolization (DEB-TACE) was superior to conventional TACE (c-TACE) due to better short-term disease control and improved progression-free survival (PFS).
- When it comes to overall survival rate, there is not enough evidence to suggest that DEB-TACE is more advantageous than c-TACE.

**What is known and what is new?**

- TACE is the primary treatment approach for intermediate to advanced-stage unresectable hepatocellular carcinoma (uHCC).
- In situations where randomized controlled trials are difficult to implement, propensity score matching is a relatively reliable alternative research method.

**What is the implication, and what should change now?**

- The detailed mechanism that the short-term disease control advantage did not convert into a survival advantage over time deserve further investigation.

## Methods

### *Patients*

Clinical data of uHCC patients who underwent c-TACE or DEB-TACE as first-line treatment in The First Affiliated Hospital of Xinjiang Medical University between September 2016 and July 2021 were retrospectively analyzed. HCC was diagnosed according to the Guidelines for Diagnosis and Treatment of Primary Liver Cancer released by the National Health Commission. Inclusion criteria were: (I) liver function classified as Child-Pugh A or B; (II) target lesions of HCC not previously treated with surgical resection, radiofrequency ablation, and TACE; (III) Eastern Cooperative Oncology Group performance status (ECOG PS) score of 0 to 1 within the week before enrollment. Exclusion criteria were: (I) liver function classified as Child-Pugh C; (II) patients unable to undergo tumor response evaluation according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST), e.g., lesions <1 cm, lesions not amenable to repeated measurements, and lesions not showing intra-tumoral arterial enhancement on contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI); (III) diffuse or distant extensive metastasis of the tumor with expected survival <3 months; (IV) patients lost to follow-up or with incomplete clinical data.

The study was conducted in accordance with the

 

Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of The First Affiliated Hospital of Xinjiang Medical University (No. 211129-04) and informed consent was taken from all the patients.

### *Interventions*

All patients underwent routine blood tests, routine biochemical tests, coagulation function and alpha-fetoprotein tests, as well as enhanced CT or enhanced MRI tests before surgery. Patients and their families were informed of the purpose of the surgical treatment and possible postoperative complications before the treatment. Informed consent was signed before surgery.

All procedures were performed by attending physicians or qualified professionals with long experience in DEB-TACE and c-TACE procedures. Before chemoembolization, celiac artery or common hepatic artery angiography was performed to assess the vascular anatomy, tumor vascularity, and the extent of the tumor. Detailed analysis of the angiographic manifestations was performed to define the tumor site, size, number, and condition of blood-supplying arteries. If scarcity/lack of vascular or incomplete tumor staining was found in some areas of the liver, imaging of the superior mesenteric artery, renal artery, left gastric artery, phrenic artery, intercostal/subcostal artery, internal thoracic artery, and lumbar artery were performed to discover the ectopic origins of hepatic arteries or collateral branches of the extrahepatic arteries for the feeder's vessels.

### *Preparation of drug-eluting microspheres and DEB-TACE treatment*

Each vial of drug-eluting microspheres (DC Bead™, Biocompatibles UK Limited, a BTG group company, UK) was loaded with 75 mg of doxorubicin (at a concentration of not less than 20 mg/mL), which was diluted with sterilized water for injection into the syringe. The 20 mL syringe containing microspheres was connected to the 5 mL syringe containing pirarubicin using a three-way valve and mixed gently several times. The loading time was 30–45 min, and the syringe was gently rolled and turned over 10 times per 10–15 min. After loading, the microspheres were mixed with sterilized water and a nonionic contrast agent to achieve a homogeneous suspension.

The microcatheter was used to super-select the blood-supplying artery of the tumor. After confirming the correct location, the mixed homogeneous suspension of drug-loaded microspheres, chemotherapeutic drugs, and contrast agents were injected into the tumor-supplying artery at a slow and steady flow rate (1 mL/min). According to the tumor blood supply situation, the flow rate of the homogeneous suspension containing chemotherapeutic drugs and contrast agents was observed to embolize branch by branch and to stop the push when the end point of embolization was achieved. Following the international common standard, achieving 3–4 cardiac cycles without emptying of the contrast agent can be regarded as a complete embolization rather than a stagnation of the blood flow. Once the initial stagnation was achieved, it was left stationary for 5 min to allow the drug-loaded microspheres to redistribute within the tumor and be pushed further distally by the blood flow. If tumor staining was still present on postoperative imaging, embolization was performed with appropriate supplementation of blank microspheres until the end point of embolization was achieved (disappearance of tumor staining).

### *c-TACE treatment*

The microcatheter was used to super-select the target segment or sub-segment of the blood supply artery. Oxaliplatin (85 mg/m$^2$) was diluted in 5% dextrose 150–200 mL and then slowly injected into the target blood vessel. The perfusion time of the drug was ≥20 min. Then, a mix of doxorubicin (30 mg/m$^2$) and iodized oil (the maximum dosage of not more than 20 mL) was injected. Under fluoroscopy, the injection was stopped based on the deposition of iodized oil in the tumor area, whether there were small branching images of the portal vein in the periphery of the tumor, and whether the iodized oil was retained in the blood vessels or if there was reflux. If a large tumor was present, the gelatin sponge particles embolization agent was chosen to enhance the embolization effect. The treatment was carried out by fractionated embolization based on the patient's condition.

### *Observation and follow-up criteria*

Postoperative patient responses were closely monitored. Common embolic syndromes included nausea, vomiting, abdominal pain, and fever. The symptoms were recorded and treated in a timely manner. According to different comprehensive treatment protocols, appropriate antiviral therapy and systemic anti-tumor therapy were given. The patient was discharged after symptomatic relief or if the patient did not have definite adverse effects.

 

Postoperative patients were monitored monthly with enhanced CT or MRI and laboratory tests (alpha-fetoprotein, blood cells count, liver function, coagulation, etc.). For those evaluated as having complete response (CR) according to the mRECIST evaluation criteria, TACE was not performed, and regular reviews were conducted. Conversely, if patients were evaluated as having partial response (PR) or progressive disease (PD), and if their liver function, physical status, and other general conditions were consistent with the requirements for the TACE procedure, then TACE treatment was performed. In the DEB-TACE group, only the first two treatments were performed with drug-eluting microspheres, and all repeat procedures were performed with lipiodol for tumor recurrence during the entire follow-up period. After the tumor was confirmed to be progression-free, patients were reviewed every three months.

According to the mRECIST evaluation criteria, tumor response was assessed and classified into CR, PR, stable disease (SD), and PD. The main observational indicators were progression-free survival (PFS), with secondary observational indicators being objective response rate (ORR) and disease control rate (DCR). Adverse events in postoperative patients were evaluated and recorded according to the Common Terminology Criteria for Adverse Events 4.0 (CTCAE 4.0). The last follow-up was July 31, 2022, or death.

### *Statistical analysis*

Given the differences in the baseline characteristics between eligible participants in the two groups (*Table 1*), propensity-score matching was used to identify a cohort of patients with similar baseline characteristics. The propensity score is a conditional probability of having a particular exposure (DEB-TACE versus C-TACE) given a set of baseline measured covariates. The propensity score was estimated with the use of a non-parsimonious multivariable logistic-regression model. PSM macro in SPSS 22.0 was used for PSM analysis. The 1:1 matching between the two groups was achieved using caliper matching, with a caliper value set at 0.03. Based on previous studies (7,8), variables were selected for inclusion in the propensity model, including age, gender, alpha-fetoprotein, ECOG score, Child-Pugh classification, tumor count, and tumor size. After adjusting for these factors, SPSS 22.0 was utilized again for data processing. Measurement data were compared using the *t*-test while counting data were compared using the chi-squared test. The Kaplan-Meier method was used to evaluate tumor progression time in the two groups, with $P<0.05$ indicating statistically significant differences.

## Results

### *Patients baseline*

Between September 2016 and July 2021, 29 patients underwent DEB-TACE and 84 received c-TACE. After 1:1 matching, 56 patients were included in the analysis. The baseline characteristics of patients before matching are shown in *Table 1*. A statistically significant difference was observed between the two groups in the number of tumors (P=0.047). There were no statistically significant differences in age, gender, alpha-fetoprotein, Barcelona Clinic Liver Cancer (BCLC) stage, ECOG PS score, or tumor size.

The baseline characteristics of patients after matching are presented in *Table 2*. There were also no statistically significant differences in age, gender, BCLC stage, ECOG score, number of tumors, or tumor size between the two groups.

### *Survival*

The median follow-up time was 22.5 months in the DEB-TACE group and 14.5 months in the c-TACE group. The median PFS in the DEB-TACE group was 10 months (95% CI, 7.1–12.9), which was significantly higher than that in the c-TACE group [6 months (95% CI, 3.8–8.2), P=0.27; *Figure 1A*]. The median OS in the DEB-TACE group was 23 months (95% CI, 17.3–28.7), while in the c-TACE group, it was 14 months (95% CI, 9.8–18.1); yet, the difference was not statistically significant (P=0.002, *Figure 1B*).

### *Treatment response*

Based on the mRECIST criteria, tumor response was evaluated 1, 3, 6, and 12 months after the procedure (*Table 3*). The ORR at 1, 3, 6, and 12 months in the DEB-TACE group was 69%, 78%, 60%, and 52%, respectively, and the DCR was 100%, 95%, 82%, and 78%, respectively. In the c-TACE group, the ORR at 1, 3, 6, and 12 months was 39%, 39%, 26%, and 8%, respectively, and the DCR was 86%, 73%, 73%, and 60%, respectively. The ORR at 1, 3, 6, and 12 months was significantly higher in the DEB-TACE group compared to the c-TACE group (all P<0.05). The DCR at 3 months was also significantly higher in the

 

**Table 1** Baseline characteristics of study patients undergoing TACE

| Variable | DEB-TACE | c-TACE | P |
|---|---|---|---|
| No. | 29 | 84 | |
| Age (years) | 57 [31–84] | 58 [33–80] | 0.78 |
| Gender | | | 0.11 |
| Male | 26 (89.66) | 82 (97.62) | |
| Female | 3 (10.34) | 2 (2.38) | |
| Cause | | | 0.76 |
| HBV | 26 (89.66) | 76 (90.47) | |
| HCV | 2 (6.90) | 4 (4.76) | |
| Alcoholism | 0 | 1 (1.20) | |
| Other | 1 (3.45) | 3 (5.57) | |
| Child-Pugh class | | | 0.68 |
| A | 28 (96.56) | 78 (92.86) | |
| B | 1 (2.44) | 6 (7.14) | |
| ECOG PS | | | 0.66 |
| 0 | 16 (55.17) | 52 (61.90) | |
| 1 | 13 (44.83) | 32 (39.10) | |
| BCLC stage | | | 0.21 |
| A | 3 (10.34) | 22 (26.19) | |
| B | 10 (34.48) | 24 (28.57) | |
| C | 16 (55.17) | 38 (45.24) | |
| No. of tumors | | | 0.047 |
| ≤3 | 6 (20.69) | 35 (41.67) | |
| >3 | 23 (79.31) | 49 (58.33) | |
| Maximal tumor size (cm) | 7.72 [2–16] | 7.29 [1–17] | 0.64 |
| AFP level (ng/mL) | | | 0.82 |
| ≤400 | 20 (68.97) | 60 (71.43) | |
| >400 | 9 (31.03) | 24 (28.57) | |

Data are presented as n (%) or median [IQR]. TACE, transarterial chemoembolization; DEB-TACE, drug-eluting beads-TACE; c-TACE, conventional TACE; HBV, hepatitis B virus; HCV, hepatitis C virus; ECOG PS, Eastern Cooperative Oncology Group performance status; BCLC, Barcelona Clinic Liver Cancer; AFP, alpha-fetal protein; IQR, interquartile range.

DEB-TACE group (P<0.05).

Target lesions were evaluated using the mRECIST criteria. There were four cases of CR, 14 cases of PR, and 10 cases of SD in the DEB-TACE group, and one case of CR, 8 cases of PR, 13 cases of SD, and six cases of PD in the c-TACE group (*Figure 2*).

### *Safety profiles*

The main postoperative adverse reaction after TACE in both groups was post-embolization pain, fever, vomiting, or nausea. The incidence rate of adverse reactions in both the DEB-TACE group and c-TACE group was 78.3%, and

 

**Table 2** Baseline characteristics of study patients undergoing TACE (after PSM analysis)

| Variable | DEB-TACE | c-TACE | P |
|---|---|---|---|
| No. | 28 | 28 | |
| Age (years) | 63 [33–84] | 58 [45–73] | 0.70 |
| Gender | | | 0.65 |
| Male | 26 (92.86) | 25 (89.29) | |
| Female | 2 (7.14) | 3 (10.71) | |
| Cause | | | 0.65 |
| HBV | 26 (92.86) | 25 (89.29) | |
| HCV | 1 (3.57) | 2 (7.14) | |
| Alcoholism | 0 | 0 | |
| Other | 1 (3.57) | 1 (3.57) | |
| Child-Pugh class | | | >0.99 |
| A | 27 (96.43) | 27 (96.43) | |
| B | 1 (3.57) | 1 (3.57) | |
| ECOG PS | | | 0.46 |
| 0 | 16 (57.14) | 14 (50.00) | |
| 1 | 12 (42.86) | 14 (50.00) | |
| BCLC stage | | | 0.85 |
| A | 3 (10.71) | 3 (10.71) | |
| B | 8 (28.57) | 7 (25.00) | |
| C | 17 (60.71) | 18 (64.29) | |
| No. of tumors | | | >0.99 |
| ≤3 | 6 (21.43) | 6 (21.43) | |
| >3 | 22 (78.57) | 22 (78.57) | |
| Maximal tumor size (cm) | 8.13 [2–16] | 7.56 [2–16] | 0.61 |
| AFP level (ng/mL) | | | 0.59 |
| ≤400 | 19 (67.86) | 17 (60.71) | |
| >400 | 9 (32.14) | 11 (39.29) | |

Data are presented as n (%) or median [IQR]. TACE, transarterial chemoembolization; PSM, propensity score matching; DEB-TACE, drug-eluting beads-TACE; c-TACE, conventional TACE; HBV, hepatitis B virus; HCV, hepatitis C virus; ECOG PS, Eastern Cooperative Oncology Group performance status; BCLC, Barcelona Clinic Liver Cancer; AFP, alpha-fetal protein; IQR, interquartile range.

most of the patients had mild adverse reactions, which were mainly grade I and II adverse reactions. After symptomatic treatment, the patients' conditions were improved. One case of postoperative liver abscess was observed in the DEB-TACE group, which was treated by puncture and drainage, after which the patient's condition improved. There were no grade IV adverse events (see *Table 4*).

## Discussion

TACE has been widely used for treating unresectable malignant liver tumors and is the only arterial treatment method proven to have survival advantages in randomized trials (9,10). Numerous studies (11-13), including prospective randomized trials, retrospective studies, and

 

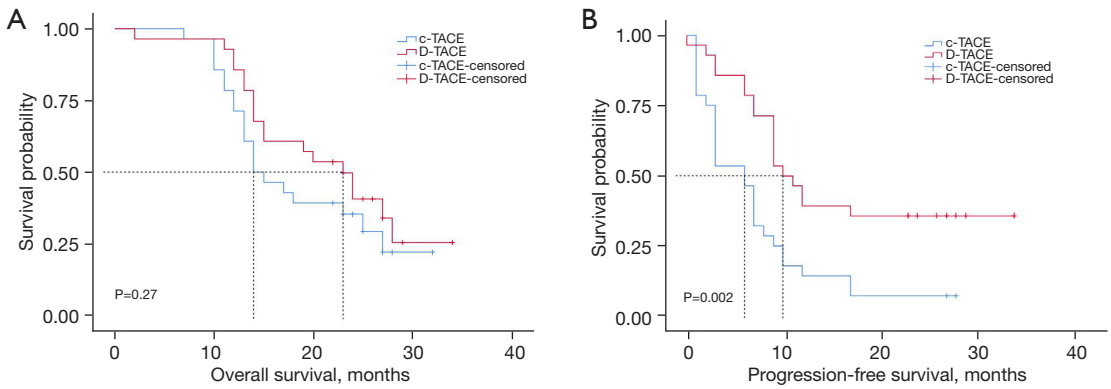


**Figure 1** Comparison of OS and PFS between DEB-TACE and c-TACE by Kaplan-Meier method in patients after PSM. (A) Refer to OS analysis after PSM; (B) refer to PFS analysis after PSM. OS, overall survival; PFS, progression-free survival; DEB-TACE, drug-eluting beads-transarterial chemoembolization; c-TACE, conventional transarterial chemoembolization; PSM, propensity score matching.

**Table 3** Comparison of ORR and DCR between DEB-TACE and c-TACE in patients after PSM

| Time after TACE | ORR | | | | DCR | | | |
|---|---|---|---|---|---|---|---|---|
| | DEB-TACE (%) | c-TACE (%) | $\chi^2$ | P | DEB-TACE (%) | c-TACE (%) | $\chi^2$ | P |
| 1 month | 69 | 39 | 4.293 | 0.04 | 100 | 86 | 3.209 | 0.07 |
| 3 months | 78 | 39 | 7.263 | 0.007 | 95 | 73 | 4.212 | 0.04 |
| 6 months | 60 | 26 | 5.662 | 0.02 | 82 | 73 | 0.511 | 0.48 |
| 12 months | 52 | 8 | 10.268 | 0.001 | 78 | 60 | 1.643 | 0.20 |

ORR, objective response rate; DCR, disease control rate; DEB-TACE, drug-eluting beads-transarterial chemoembolization; c-TACE, conventional transarterial chemoembolization; PSM, propensity score matching.

meta-analyses, have compared the safety and efficacy of DEB-TACE treatment and c-TACE for uHCC, reporting conflicting results. A single-center prospective phase II study (11) that included patients treated with c-TACE and DEB-TACE for uHCC showed that although tumor response was similar, the toxicity profile of DEB-TACE was superior to c-TACE. A recent retrospective analysis (12) of the efficacy and safety in Chinese HCC patients found that patients treated with c-TACE had a significantly higher recurrence rate at 6 months compared to DEB-TACE (43.3% *vs.* 16.7%; P=0.04). This suggests that DEB-TACE have better near-term efficacy than c-TACE in treating Chinese patients with HCC and possess a lower complication rate.

In contrast, Massani *et al.* (13) analyzed 82 non-surgical patients treated with either c-TACE or DEB-TACE with a 12-month follow-up and evaluated by CT postoperatively and found a median survival of 22.7 months in the DEB-TACE group compared to 21.8 months in the c-TACE group (12). These results suggest that DEB-TACE is as effective as c-TACE in treating HCC, with better tolerance. There was no difference in survival between both treatment techniques, and both could be performed in the event of tumor recurrence without significantly increasing the risk of surgical complications and liver failure.

Due to the lack of an inherent "balance principle" in RCTs, retrospective observational studies are limited by various biases and confounding factors. These limitations affect the reliable comparison of outcomes between the experimental and control groups. Therefore, utilizing PSM analysis to balance confounding factors and eliminate bias is a method that ensures even distributions of confounding factors between groups, enhances group comparability and allows for a direct estimation of treatment effects (14). In order to make the test results more credible, the PSM method is primarily employed in retrospective analysis studies, where there are more subjects in the control group compared to the experimental group and numerous

 

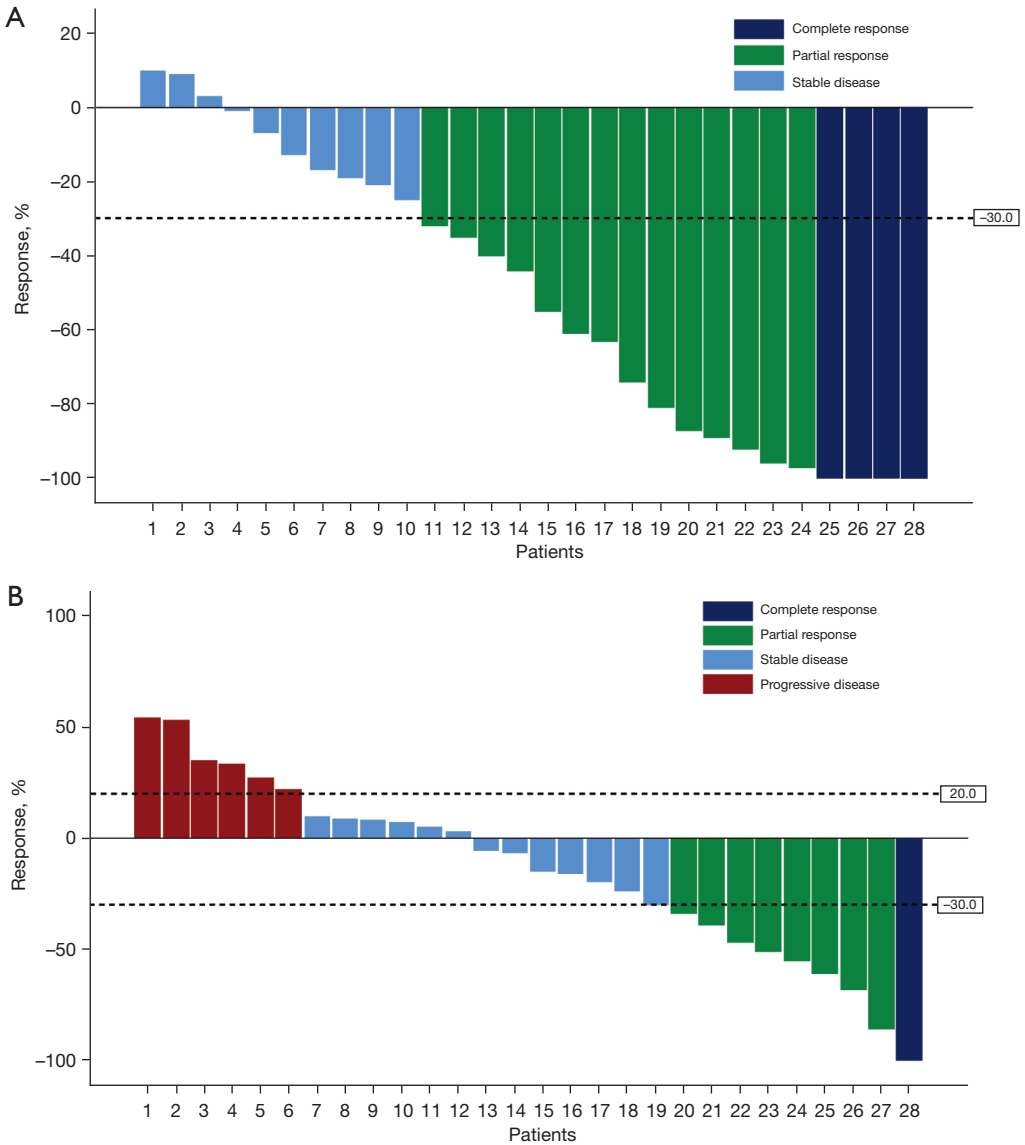


**Figure 2** Waterfall plot of changes in tumor size according to the mRECIST criteria. (A) According to mRECIST criteria, 4 cases of CR, 14 cases of PR, and 10 cases of SD in the DEB-TACE group; (B) according to mRECIST criteria, 1 case of CR, 8 cases of PR, and 13 cases of SD in the c-TACE group. mRECIST, modified response evaluation criteria in solid tumors; CR, complete response; PR, partial response; SD, stable disease; DEB-TACE, drug-eluting beads-transarterial chemoembolization; c-TACE, conventional transarterial chemoembolization.

confounding factors that are challenging to control.

Since multiple factors affect the efficacy of TACE in HCC treatment, such as liver function classification, staging, tumor size, and number of tumors (15), this study applied PSM to balance patients' baseline characteristics and retrospectively analyzed the clinical outcomes of DEB-TACE and c-TACE in the treatment of primary HCC. The results suggested that DEB-TACE was superior to c-TACE due to better short-term disease control and improved PFS (10 *vs.* 6 months, P=0.002). However, this short-term disease control advantage did not convert into a survival advantage over time. Furthermore, even though the median OS was slightly higher in the DEB-TACE group than in the c-TACE group, the observed difference was not statistically significant.

The contradictory phenomenon of short-term versus

 

**Table 4** Safety profiles

| AE | DEB-TACE (N=28) | | | | c-TACE (N=28) | | | |
|---|---|---|---|---|---|---|---|---|
| | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
| Fever | 10 (35.7) | 3 (10.7) | 0 | 0 | 6 (21.4) | 3 (10.7) | 0 | 0 |
| Pain | 14 (50.0) | 5 (17.9) | 0 | 0 | 11 (39.3) | 5 (17.9) | 0 | 0 |
| Nausea | 2 (7.1) | 0 | 0 | 0 | 3 (10.7) | 1 (3.6) | 0 | 0 |
| Hepatapostema | 0 | 0 | 1 (3.6) | 0 | 0 | 0 | 0 | 0 |
| Anorexia | 3 (10.7) | 0 | 0 | 0 | 4 (14.3) | 0 | 0 | 0 |
| Fatigue | 4 (14.3) | 0 | 0 | 0 | 5 (17.9) | 0 | 0 | 0 |
| AST elevation | 9 (32.1) | 2 (7.1) | 0 | 0 | 11 (39.3) | 2 (7.1) | 0 | 0 |
| ALT elevation | 9 (32.1) | 2 (7.1) | 0 | 0 | 11 (39.3) | 2 (7.1) | 0 | 0 |
| Bilirubin elevation | 4 (14.3) | 0 | 0 | 0 | 5 (17.9) | 0 | 0 | 0 |

Data are presented as n (%). AE, adverse event; DEB-TACE, drug-eluting beads-transarterial chemoembolization; c-TACE, conventional transarterial chemoembolization; AST, aspartate transaminase; ALT, alanine transaminase.

long-term benefits may be attributed to the following: (I) with the development of targeted and immune therapies, the survival of HCC patients is gradually extended (16-18); these patients often receive various forms of systemic treatment alongside TACE, which can weaken the benefits of various TACE methods, especially the long-term benefits; (II) the pronounced short-term benefit of DEB-TACE might be related to the pharmacokinetics of drug-eluting microspheres, allowing for higher doses of chemotherapy drugs within the tumor and prolonged contact time with cancer cells. Additionally, choosing 100–300 μm or smaller diameter drug-eluting microspheres might be an important factor since smaller microspheres can induce extensive necrosis in target lesions due to their ability to achieve more distal and complete embolization and more effectively block collateral vessels (19).

Regarding safety comparison, adverse events primarily manifested as post-embolization syndrome in both groups, with no difference in incidence (78.26%). Post-procedure liver abscess occurred in one patient in the DEB-TACE group, which might be associated with tissue necrosis caused by embolization of arterial endings by microspheres. Overall, there were no significant differences in safety profiles between groups.

The present study has a few limitations. First, this study had a relatively small sample size. Second, although the PSM method was used in this trial, the shortcomings of the retrospective analysis method were still unavoidable and factors outside the model were not taken into account. Finally, this is a single-center study, and the heterogeneity of TACE operations, especially c-TACE operations, may lead to some differences in the study findings compared with other centers. Therefore, larger multicenter controlled trials are needed to confirm the efficacy of DEB-TACE in the treatment of primary HCC.

## Conclusions

In conclusion, this study demonstrates that DEB-TACE can extend PFS and achieve better short-term ORR with similar safety profiles compared to c-TACE in treating uHCC. However, there is no significant advantage in OS.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-369/rc

*Data Sharing Statement:* Available at https://jgo.amegroups.

 

com/article/view/10.21037/jgo-24-369/dss

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-369/coif). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of The First Affiliated Hospital of Xinjiang Medical University (No. 211129-04). The patients provided the written informed consent to participate in this study.



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