Comprehensive Analysis of Factors Affecting Clinical Response and Short-Term Survival to Drug-Eluting Bead Transarterial Chemoembolization for Treatment in Patients With Liver Cancer

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Abstract
This study aimed to investigate the clinical response and short-term survival and further explore the comprehensive factors for predicting clinical outcomes in patients with liver cancer treated by drug-eluting beads transarterial chemoembolization. Forty-nine patients with liver cancer who received drug-eluting beads transarterial chemoembolization treatment were consecutively enrolled in this cohort study. Demographic features, medical histories, clinicopathological properties, biochemical indexes, previous treatments, and chemoembolization reagents were recorded. Ten (20.4%) patients achieved complete response and 31 (63.3%) patients achieved partial response after drug-eluting beads transarterial chemoembolization treatment, with overall response rate of 83.7%. Logistic analysis revealed that high aspartate aminotransferase \((P = .041)\), high carbohydrate antigen 199 \((P = .030)\), and low hemoglobin \((P = .020)\) could independently predict less possibility for complete response achievement. As to survival analysis, high alkaline phosphatase \((P = .040)\), low albumin \((P = .033)\) low hemoglobin \((P = .018)\), portal vein invasion \((P = .025)\), higher Eastern Cooperative Oncology Group performance status \((P = .011)\), and higher Child-pugh stage \((P = .001)\) were independent predictors for worse overall survival. In conclusion, the present study validated that drug-eluting beads transarterial chemoembolization was effective and well tolerated for patients with liver cancer, and high aspartate aminotransferase, high alkaline phosphatase, low albumin, low hemoglobin, portal vein invasion, higher Child-pugh stage, higher Barcelona Clinic Liver Cancer stage, higher Eastern Cooperative Oncology Group performance status were correlated with worse outcomes.

Keywords
drug-eluting beads transarterial chemoembolization (DEB-TACE), clinical response, overall survival, predictive factors, liver cancer

Abbreviations
AFP, alpha-fetoprotein; BCLC, Barcelona Clinic Liver Cancer; BUN, blood urea nitrogen; cTACE, conventional TACE; CEA, carcino-embryonic antigen; CA199, carbohydrate antigen 199; CR, complete response; CBDOX, CBs loaded with doxorubicin; DEB-TACE, drug-eluting beads transarterial chemoembolization; ECOG, Eastern Cooperative Oncology Group; HCC, hepatocellular carcinoma; ICC, intrahepatic cholangiocarcinoma; K-M, Kaplan-Meier; ORR, overall response rate; PR, partial response; PD, progressed disease; SD, stable disease.

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Introduction

Liver cancer, as one of the malignant tumors and the second leading cause of cancer deaths in men of less developed countries, is a crucial threat imperiling human health worldwide.\(^1\,2\) The 2015 Global cancer statistics report discloses that roughly 0.78 million people were diagnosed with liver cancer contributing to 6% of new patients with cancer over the world in 2012, and approximately 0.75 million patients died from liver cancer accounting for 9% deaths in all cancers, among which half of the new liver cancers and deaths derives from China.\(^2\)

Despite the great improvements in early diagnosis, targeted therapies, immune therapies, personalized treatments as well as integrated patients' care, the prognosis of both hepatocellular carcinoma (HCC, 70%-90% of all liver cancers) and intrahepatic cholangiocarcinoma (ICC), as 2 main categories of liver cancers, is still far more from satisfaction.\(^3\,7\)

Transarterial chemoembolization (TACE), as a first-line treatment for HCC in intermediate stage that was recommended by Barcelona Clinic Liver Cancer (BCLC) tumor staging and management, is recently widely utilized as a common modality in patients with HCC, especially for patients unsuitable to receive surgery and/or ablation.\(^8\,10\) Due to severe cytotoxic effect combined with ischemia, lack of calibrated operative techniques and heterogeneities according to chemotherapeutic agents, treatment devices, and schedule, conventional TACE (cTACE) is gradually replaced by drug-eluting beads (DEB)-TACE gradually in clinical practice, which better standardizes the procedure and improves the delivering capacity of higher dose of chemotherapy agents.\(^11\,13\)

Multiple previous studies have explored the predictive factors for clinical response or long-term survival in patients treated with cTACE.\(^14\,17\) However, few studies evaluating prognostic biomarkers for DEB-TACE treatment have been carried out. Therefore, this study aimed to investigate the clinical response and short-term survival and further explore the comprehensive factors in predicting clinical outcomes in patients with liver cancer treated by DEB-TACE.

Materials and Methods

Patients

Forty-nine patients with hepatic tumor in Sir Run Run Shaw Hospital from January 2016 to November 2016 were enrolled in this cohort study. The inclusion criteria were as follows: (1) patients diagnosed with HCC, intrahepatic cholangiocarcinoma (ICC), or secondary hepatic tumor via pathologic assessment or noninvasive diagnostic criteria according to American Association for the Study of the Liver Diseases (AASLD) guidelines,\(^18\) (2) age older than 18 years, and (3) patients were about to receive DEB-TACE treatment by clinical demand. Meanwhile, the exclusion criteria were as follows: (1) patients who received previous liver transplantation, (2) patients who lacked histological grade information, (3) patients with incomplete laboratory values, (4) patients with contraindication for artery puncture, (5) patients with severe liver failure or kidney failure, (6) patients with cognitive impairment or unable to understand the study consents, and (7) women who were in gestation or lactation period.

This study was approved by the Ethical Committee of Sir Run Run Shaw Hospital, and all written informed consents from patients were obtained. Moreover, this study was performed according to the Declaration of Helsinki.

Drug-Eluting Beads Transarterial Chemoembolization Procedure

Drug-eluting beads transarterial chemoembolization was performed in all patients on demand, the indication of which was determined by the assessment of multidisciplinary teamwork. CalSiSpheres beads (CBs; Jiangsu Hengrui Medicine Co, Ltd, Jiangsu, China) with the diameter ranging from 100 to 300 µm were used as carriers. Bead loading was conducted using adriamycin drug (adriamycin, pirarubicin, or epirubicin) 50 to 80 mg, and the mean dose was 60 mg for patients with primary liver cancer. In terms of patients with secondary liver cancer, the bead loading was performed using irinotecan 100 mg. Chemotherapy reagent was made to 20 mg/mL solution extracted by a 10 mL injector for further application. The CBs were shaken up, subsequently the bead suspension was extracted into a 20 mL injector and placed for 5 minutes, and the liquid supernatant was pulled out of the injector. The chemotherapy reagent solution and CBs were mixed continuously in a 20-mL injector and shaken up every 5 minutes and placed for 30 minutes in room temperature at 23°C to 28°C. Finally, nonionic contrast agent was administered at the ratio of 1:1, and the mixture was placed for another 5 minutes in room temperature at 23°C to 28°C for use. For tumors that did not reach the embolization end point after a bottle of CBs was emptied, ordinary embolization agents were utilized.

The DEB-TACE was performed under local anesthesia. Hepatic angiography was performed to detect the tumor-supplying vessels, and microcatheter (MC-PE27131, Terumo, Japan) was used for the embolization of tumor-supplying vessel. The CB mixture with contrast agent was pulsed injected to vessel at the rate of 1 mL/min, and the injection was stopped when the flow of contrast agent slowed down. After 5 minutes, the angiography was conducted for the second time, and the embolization was continued if tumor blush still existed until all blushed tumors vanished. If there were still blushed, tumors existed when a bottle of CBs was emptied, the embolization was continued using Embosphere beads until there was no more blushed tumors. Subsequently, the microcatheter was pulled out, and the hemostasis by compression was performed, and the punctured wound was bound up. All patients postembolization were told to lie on one side and extend the punctured leg for 6 to 12 hours.

Post-DEB-TACE Treatment

Patients with postoperative nausea and vomiting were treated with an intravenous injection of tropisetron and ondansetron.
Pethidine, dexamethasone, and lidocaine were given as analgesic treatment for pain. In addition, patients with infection were treated with sulperazone 2 mg/ every 12 hours and levofloxacin.

Clinical and Pathological Features

Comprehensive baseline properties of patients were collected to analyze their predictive values for clinical outcomes, which included (1) demographic features: age and gender; (2) medical history: hepatic B virus hepatitis, drink, and cirrhosis; (3) clinicopathological features: histology, tumor distribution, largest nodule size, tumor location, portal vein invasion, hepatic vein invasion, Eastern Cooperative Oncology Group (ECOG) performance status, child-pugh stage, and Barcelona Clinic Liver Cancer (BCLC) Stage; (4) biochemical indexes: while blood cell, red blood cell, absolute neutrophil count, hemoglobin, platelet, albumin (ALB), total protein, total bilirubin, total bile acid, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, blood creatinine, blood urea nitrogen (BUN), alpha-fetoprotein (AFP), carcino-embryonic antigen (CEA), and carbohydrate antigen199 (CA199); (5) previous treatments: cTACE, surgery, systematic chemotherapy, radiofrequency ablation, and targeted therapy; (6) chemoembolization reagents: adriamycin drug and irinotecan; and (7) combination of ordinary embolization agent.

Definitions and Follow-Ups

The imaging response including computerized tomography and magnetic resonance imaging as well as blood test results were recorded. Imaging response was assessed according to modified Response Evaluation Criteria in Solid Tumors (mRECIST) 19: (1) complete response (CR)—no existence of arterial enhancement of targeted tumors; (2) partial response (PR)—decrease in diameter of targeted tumor (with arterial enhancement) <30%; (3) stable disease (SD)—decrease in diameter of targeted tumor (with arterial enhancement) did not achieve PR or less than PD; and (4) progressive disease (PD)—increase in diameter of targeted tumor (with arterial enhancement) ≥20% or new tumor existed. Overall response rate (ORR) was defined as the portion of patients who achieved CR and PR. In addition, the clinical response was evaluated at 1 to 3 months after DEB-TACE. Overall survival (OS) was calculated from the time of DEB-TACE operation to the date of death or last follow-up. Safety was assessed according to the count and percentage of adverse events after DEB-TACE. The median follow-up duration was 120 (range from 30 to 236) days, and the last follow-up date was December 12, 2016.

Statistics

Statistical analysis was performed using SPSS 22.0 software (IBM, USA). Data were presented as count (%), mean (standard deviation), or median (25th-75th). Logistic regression and Cox proportional hazards regression were performed to evaluate the predicting factors for CR, ORR, and OS of patients. Kaplan-Meier (K-M) curves were conducted to analyze OS in patients with different clinicopathological features or laboratory values. $P < .05$ was considered significant.

Results

Characteristics

Forty-nine patients treated using DEB-TACE with mean age 59.95 ± 11.38 years were included in this study, of which 38 (77.6%) cases were male and 11 (22.4%) cases were female. Thirty-eight (77.5%) cases were patients with primary HCC, 2 (4.1%) cases were patients with primary ICC, while 9 (18.4%) cases were patients with secondary hepatic tumor. Thirty-two (65.3%) patients were multifocal and 17 (34.7%) patients were unifocal, with median largest nodule size of 5.70 (3.00-8.55) cm. Portal vein invasion and hepatic vein invasion were observed in 18 (36.7%) and 10 (20.4%) patients, respectively. Besides, 35 (71.4%), 9 (18.3%), 2 (4.1%), and 3 (6.2%) patients were at ECOG performance status 0, 1, 2, and 3, respectively. With regard to the stages for primary liver cancer, 31 (77.5%) patients were categorized into Child-pugh stage A, 9 (22.5%) patients were stage B, and 24 (60%), 7 (17.5%), and 9 (22.5%) patients were at BCLC stages A, B, and C, respectively. Other detailed information about clinicopathological features, biochemical indexes, previous treatments, and combination of chemoembolization reagents and ordinary embolization agent is given in Table 1.

Clinical Response of DEB-TACE Treatment

As presented Table 2, 10 (20.4%) patients achieved CR and 31 (63.3%) patients achieved PR after DEB-TACE treatment, with ORR of 83.7%. In addition, 7 (14.3%) patients were SD, while 1 (2.0%) patient with disease progressed (PD).

Comprehensive Analysis of Factors Predicting CR and ORR

To investigate the comprehensive predictive factors affecting clinical response, univariate and multivariate logistic regression analysis were performed.

As to CR achievement, univariate analysis illuminated that high AST ($P = .041$, odds ratio [OR]: 0.174, 95% confidence interval [CI]: 0.033-0.929) and high CA199 ($P = .030$, OR: 0.156, 0.029-0.837) could predict less possibility for CR achievement, while high BUN ($P = .020$, OR: 12.937, 95% CI: 1.489-112.437) was associated with greater possibility for CR achievement (Table 3). Factors with $P$ value < .1 were further analyzed by multivariate model, and no factors had independently predicted value for CR achievement, while high BUN disclosed a potential value in predicting CR ($P = .055$, OR: 11.659, 95% CI: 0.945-143.874) but without statistical significance. However, due to the lack of CR events or non-CR events, “secondary versus primary hepatic tumor,” “multifocal versus unifocal,” “hepatic vein invasion,” “higher ECOG,” “higher child-pugh stage,” “previous systematic
Table 1. Baseline Characteristics of Patients With Liver Cancers.\(^a\)

| Parameters                      | Patients (n = 49) |
|---------------------------------|------------------|
| Age, years                      | 59.95 ± 11.38    |
| Gender, female/male             | 11/38            |
| HBV, n (%)                      | 35 (71.4%)       |
| Drink, n (%)                    | 17 (34.6%)       |
| Cirrhosis, n (%)                | 21 (42.9%)       |
| Histology                       |                  |
| Primary HCC, n (%)              | 38 (77.5%)       |
| Primary ICC, n (%)              | 2 (4.1%)         |
| Secondary hepatic tumor, n%     | 9 (18.4%)        |
| Tumor location                  |                  |
| Left liver, n (%)               | 10 (20.4%)       |
| Right liver, n (%)              | 23 (46.9%)       |
| Bilobar, n (%)                  | 16 (32.7%)       |
| Portal vein invasion, n (%)     | 18 (36.7%)       |
| Hepatic vein invasion, n (%)    | 10 (20.4%)       |
| ECOG performance status         |                  |
| 0, n (%)                        | 35 (71.4%)       |
| 1, n (%)                        | 9 (18.3%)        |
| 2, n (%)                        | 2 (4.1%)         |
| 3, n (%)                        | 3 (6.2%)         |
| Child-pugh stage (n = 40)       |                  |
| A, n (%)                        | 31 (77.5%)       |
| B, n (%)                        | 9 (22.5%)        |
| BCLC stage (n = 40)             |                  |
| A, n (%)                        | 24 (60%)         |
| B, n (%)                        | 7 (17.5%)        |
| C, n (%)                        | 9 (22.5%)        |
| Biochemical indexes             |                  |
| WBC, ×10\(^3\) cell/L           | 4.80 (3.75-6.60) |
| RBC, ×10\(^12\) cell/L          | 4.01 (3.43-4.45) |
| ANC (%)                         | 64.10 (54.70-73.60) |
| HB, g/L                         | 12.70 (11.65-14.10) |
| PLT, ×10\(^9\) cell/L           | 97.00 (54.50-137.00) |
| ALB, g/L                        | 37.20 (33.60-42.05) |
| TP, g/L                         | 66.70 (58.60-70.50) |
| TBIL, mmol/L                    | 17.10 (11.85-31.70) |
| TBA, I/L                        | 14.35 (6.70-28.38) |
| ALT, µ/L                        | 31.00 (23.50-51.00) |
| AST, µ/L                        | 40.00 (31.50-51.00) |
| ALP, µ/L                        | 147.00 (100.00-213.00) |
| BCr, mmol/L                     | 66.00 (55.00-72.50) |
| AFP, µg/L                       | 3.92 (2.93-5.33) |
| CEA, µg/L                       | 18.46 (3.15-1065.56) |
| CA199, kU/L                     | 2.74 (2.13-5.04) |
| Previous treatments             |                  |
| cTACE, n (%)                    | 15 (30.6%)       |
| Surgery, n (%)                  | 32 (65.3%)       |
| Systematic chemotherapy, n (%)  | 11 (22.4%)       |
| Radiofrequency ablation, n (%)  | 6 (12.2%)        |
| Targeted therapy, n (%)         | 2 (4.1%)         |
| Chemoembolization reagents      |                  |
| Adriamycin drug, n (%)          | 40 (81.6%)       |
| Irinotecan, n (%)               | 9 (18.4%)        |

\(^a\)Data were presented as mean (standard deviation), median (25th-75th), or count (%).

Table 2. Clinical Response of DEB-TACE Treatment in All Patients.\(^a\)

| Parameters                      | Patients (n = 49) |
|---------------------------------|------------------|
| Combination of ordinary embolization agent | 23 (46.9%) |

\(^a\)Data were presented as mean (standard deviation), median (25th-75th), or count (%).

Overall Survival Analysis

Overall survival was calculated from the date of DEB-TACE to death of patients or lost follow-up. One hundred eighty days of OS was 62.3% ± 10.5% for all patients with liver cancer. Patients were then divided into subgroups by patients’ features, and subgroup OS analysis by K-M curve and log-rank test were performed. All features associated with OS with P value < .1 by log-rank test is shown in Figure 1, which illustrated that largest nodule size ≥ 5.7 cm (P = .047, Figure 1A), portal vein...
invasion (P = .014, Figure 1C), higher ECOG performance status (P < .001, Figure 1D), higher Child-pugh stage (P < .001, Figure 1E), and high ALP (P = .026, Figure 1I) were associated with worse OS; while high ALB (P = .018, Figure 1H) and high BUN (P = .007, Figure 1J) were correlated with prolonged OS.

### Comprehensive Analysis of Factors Predicting OS

To investigate the comprehensive predictive factors affecting OS, univariate and multivariate Cox hazard ratio regression analysis were conducted.

In univariate analysis, portal vein invasion (P = .025, hazard ratio [HR]: 4.571, 95% CI: 1.210-17.266), higher...
ECOG performance status \( (P = 0.011, \text{HR: } 1.984, 95\% \text{ CI: } 1.165-3.256) \), higher Child-pugh stage \( (P = 0.001, \text{HR: } 14.266, 95\% \text{ CI: } 2.830-71.508) \), and high ALP \( (P = 0.040, \text{HR: } 4.055, 95\% \text{ CI: } 1.068-15.404) \) were factors for predicting shorter OS, while high ALB \( (P = 0.033, \text{HR: } 0.186, 95\% \text{ CI: } 0.040-0.874) \) and high BUN \( (P = 0.018, \text{HR: } 0.153, 95\% \text{ CI: } 0.032-0.723) \) could predict favorable OS (Table 5). Factors with \( P \) value < .1 were further analyzed by multivariate model, and no factors had independently predictive value for OS.

### Table 4. Predicting Factors for ORR of DEB-TACE Treatment.\(^a\)

| Predictor                                      | Univariate Logistic Regression | Multivariate Logistic Regression | 95% CI       | 95% CI       |
|------------------------------------------------|-------------------------------|---------------------------------|--------------|--------------|
| Age ≥60 years                                  | \( P = 0.051 \)               | \( OR = 8.944 \)               | 1.007-79.457 | -            |
| Gender (Female)                                | \( P = 0.471 \)               | \( OR = 2.258 \)               | 0.247-20.650 | -            |
| HBV                                            | \( P = 0.544 \)               | \( OR = 1.636 \)               | 0.334-8.019  | -            |
| Drink                                          | \( P = 0.855 \)               | \( OR = 0.864 \)               | 0.180-4.155  | -            |
| Cirrhosis\(^c\)                                |                               |                                 | -            | -            |
| Secondary vs primary hepatic tumor             | \( P = 0.599 \)               | \( OR = 0.618 \)               | 0.103-3.719  | -            |
| Multifocal vs Unifocal                         | \( P = 0.179 \)               | \( OR = 0.321 \)               | 0.109-0.939  | -            |
| Largest nodule size ≥5.7 cm                    | \( P = 0.850 \)               | \( OR = 1.158 \)               | 0.254-5.272  | -            |
| Bilobar vs Unilobar                            | \( P = 0.062 \)               | \( OR = 2.220 \)               | 0.045-1.078  | -            |
| Portal vein invasion                           | \( P = 0.009 \)               | \( OR = 0.052 \)               | 0.006-0.476  | -            |
| Hepatic vein invasion                          | \( P = 0.550 \)               | \( OR = 1.969 \)               | 0.213-18.163 | -            |
| Higher ECOG                                     | \( P = 0.519 \)               | \( OR = 0.767 \)               | 0.342-1.719  | -            |
| Higher Child-pugh stage                        | \( P = 0.013 \)               | \( OR = 0.086 \)               | 0.012-0.603  | -            |
| Higher BCLC stage                              | \( P = 0.038 \)               | \( OR = 0.094 \)               | 0.019-0.472  | -            |
| WBC >4.0.\(10^9\) cell/L                      | \( P = 0.950 \)               | \( OR = 0.952 \)               | 0.209-4.334  | -            |
| RBC >4.0.\(10^{12}\) cell/L                   | \( P = 0.154 \)               | \( OR = 3.474 \)               | 0.045-1.078  | -            |
| ANC% >64.10                                    |                               |                                 | -            | -            |
| HB >12.70, g/L                                 | \( P = 0.408 \)               | \( OR = 1.930 \)               | 0.407-9.160  | -            |
| PLT >7.00.\(10^9\) cell/L                     | \( P = 0.656 \)               | \( OR = 0.708 \)               | 0.155-3.325  | -            |
| ALB >37.20, g/L                                | \( P = 0.561 \)               | \( OR = 1.587 \)               | 0.335-7.530  | -            |
| TP >66.70, g/L                                 | \( P = 0.561 \)               | \( OR = 1.587 \)               | 0.335-7.530  | -            |
| TBIL >17.10, \(\mu\text{mol}/L\)              | \( P = 0.154 \)               | \( OR = 0.288 \)               | 0.052-1.598  | -            |
| TBA >143.5, \(\mu\text{L}\)                   | \( P = 0.408 \)               | \( OR = 1.930 \)               | 0.407-9.160  | -            |
| ALT >31.0, \(\mu\text{L}\)                    | \( P = 0.950 \)               | \( OR = 1.050 \)               | 0.231-4.778  | -            |
| AST >40.0, \(\mu\text{L}\)                    | \( P = 0.154 \)               | \( OR = 0.288 \)               | 0.052-1.598  | -            |
| ALP >147.0, \(\mu\text{L}\)                   | \( P = 0.099 \)               | \( OR = 0.236 \)               | 0.042-1.314  | -            |
| BCr >66.0, \(\mu\text{mol}/L\)                |                               |                                 | -            | -            |
| BUN >3.92, \(\mu\text{mol}/L\)                | \( P = 0.189 \)               | \( OR = 3.150 \)               | 0.568-17.477 | -            |
| AFP >18.46, \(\mu\text{g}/L\)                 | \( P = 0.950 \)               | \( OR = 1.050 \)               | 0.231-4.778  | -            |
| CEA >2.74, \(\mu\text{g}/L\)                  | \( P = 0.342 \)               | \( OR = 2.130 \)               | 0.448-10.120 | -            |
| CA199 >24.80, \(\text{kU}/L\)                 | \( P = 0.561 \)               | \( OR = 0.630 \)               | 0.133-2.989  | -            |
| Previous cTACE                                  | \( P = 0.707 \)               | \( OR = 1.393 \)               | 0.247-7.858  | -            |
| Previous surgery                                | \( P = 0.179 \)               | \( OR = 0.223 \)               | 0.025-1.989  | -            |
| Previous systematic chemotherapy                | \( P = 0.054 \)               | \( OR = 0.206 \)               | 0.041-1.027  | -            |
| Previous radiofrequency ablation               | \( P = 0.981 \)               | \( OR = 0.972 \)               | 0.098-9.645  | -            |
| Previous targeted therapy\(^a\)                |                               |                                 | -            | -            |
| Adriamycin drug(chemoembolization reagents)     | \( P = 0.599 \)               | \( OR = 1.619 \)               | 0.269-9.748  | -            |
| Irinotecan (chemoembolization reagents)         | \( P = 0.599 \)               | \( OR = 1.618 \)               | 0.103-3.719  | -            |
| Combination of ordinary embolization agent      | \( P = 0.099 \)               | \( OR = 0.236 \)               | 0.042-1.314  | -            |

Abbreviations: ANC, absolute neutrophil count; AFP, alpha fetoprotein; ALT, alanine aminotransferase; ALB, albumin; AST, aspartate aminotransferase; ALP, alkaline phosphatase; BCLC, Barcelona Clinic Liver Cancer; BUN, blood urea nitrogen; BCr, blood creatinine; CEA, carcino-embryonic antigen; CA199, carbohydrate antigen 199; cTACE, conventional transarterial chemo-embolization; ECOG, Eastern Cooperative Oncology Group; HB, hemoglobin; HBV, hepatic b virus; RBC, red blood cell; PLT, platelet; TP, total protein; TBIL, total bilirubin; TBA, total bile acid; WBC, while blood cell.

\(^a\)Data were presented as \( P \) value, OR (odds ratio), and 95\% CI. Significance was determined by univariate and multivariate logistic regression analysis. All factors with \( P \) value < .1 in univariate model were further analyzed by multivariate model. \( P \) value < .05 was considered significant.

\(^b\)Multivariate model was not available due to relative small sample (49 cases) according to too many variables (8 were included).

\(^c\)Due to the lack of ORR events or non-ORR events, “cirrhosis,” “high BUN,” and “previous targeted therapy” were not available for univariate logistic model. The boldface values stand for values with statistical significance.
Safety Profiles

Safety profiles during DEB-TACE operation and post-DEB-TACE operation are presented in Table 6. During DEB-TACE operation, pain occurred in 22 (44.9%) patients, fever in 1 (2.0%) patient, and others in 1 (2.0%) patient. After DEB-TACE operation, 31 (63.3%) patients had pain, 27 (55.1%) patients had liver dysfunction, 31 (34.7%) patients had fever, 9 (18.4%) patients had nausea, and 14 patients (28.6%) had vomiting. Each symptom was treated by clinical practice accordingly, and no SAE occurred.

Subgroup Analysis of Patients With HCC

There were a total of 38 (77.6%) patients with HCC of 49 (100.0%) patients with liver cancer enrolled in our study and are presented in Table 7. Ten (26.3%) patients achieved CR and...
Table 6. Safety Profiles of DEB-TACE Treatment in All Patients.

| Parameters                        | n (%) |
|-----------------------------------|-------|
| During DEB-TACE operation         |       |
| Pain                              | 24 (49.0%) |
| Fever                             | 22 (44.9%) |
| Nausea                            | 1 (2.0%) |
| Vomiting                          | 0 (0.0%) |
| Others                            | 1 (2.0%) |
| After DEB-TACE operation          |       |
| Pain                              | 46 (93.9%) |
| Fever                             | 31 (63.3%) |
| Nausea                            | 17 (34.7%) |
| Vomiting                          | 9 (18.4%) |
| Liver dysfunction                 | 14 (28.6%) |
| Alopecia                          | 27 (55.1%) |
| Chromatosis                       | 0 (0.0%) |
| Alopecia                          | 0 (0.0%) |
| Bone marrow toxicity              | 6 (12.2%) |
| Others                            | 3 (6.1%) |

Abbreviation: DEB-TACE, drug-eluting beads transarterial chemoembolization.
*Data were presented as count (%).

Table 7. Clinical Response of DEB-TACE Treatment in Patients With HCC.

| Parameters             | n (%) |
|------------------------|-------|
| Total patients         | 38 (100.0%) |
| CR                     | 10 (26.3%) |
| PR                     | 23 (60.5%) |
| ORR                    | 33 (86.8%) |
| SD                     | 4 (10.5%) |
| PD                     | 1 (2.6%) |

Abbreviations: CR, complete response; ORR, overall response rate; PD, progress disease; PR, partial response; SD, stable disease.
*Data were presented as count (%).

In the present study, we found (1) 83.7% patients with liver cancer achieved ORR by DEB-TACE treatment with tolerable side effects. (2) Comprehensive analysis revealed that patients with baseline high AST, high CA199, portal vein invasion, higher Child-pugh stage, and higher BCLC stage were seemed to less likely achieve clinical response, while high BUN could predict a increased possibility for achieving clinical response. (3) Portal vein invasion, higher ECOG performance status, higher Child-pugh stage, and high ALP were predictors for shorter OS, while high ALB and high BUN could predict favorable OS.

Liver cancer, with poor prognosis on account of late diagnosis and heterogeneity, is one of the most severe solid tumors worldwide, which mainly consists of HCC. In order to better improve the outcomes of liver cancers, BCLC staging and management divided the HCC into several stages by risk evaluation, in which TACE treatment is recommended as first-line treatment for intermediate HCC. Transarterial chemoembolization is carried out in many patients with early-stage HCC who are unsuitable for curative treatment due to physical condition, surgical contraindication, and so on, which account for nearly half of total cases with TACE. In line with the previous clinical experience, our study mainly included patients with BCLC stages A and B treated by DEB-TACE in the real-world setting.

Transarterial chemoembolization is categorized into cTACE and DEB-TACE. Recently, cTACE was gradually replaced by DEB-TACE due to the inconsistency in the technique and treatment schedule, and a large proportion of chemoembolization drugs may flow into the circulatory system subsequently inducing systemic toxicity in the duration between chemotherapy injection and embolic agent placement. DEB-TACE, first proposed in 2006 as commercial application, better standardizes the procedure, decreases treatment sessions,
stabilizes the efficacy, builds up the drug-delivering capacity as well as reduces systemic toxicity technically.11-13,23,24 However, the objective clinical benefit of DEB-TACE compared to cTACE are still controversial, and a great amount of studies illuminated that DEB-TACE does not improve the clinical response or survival compared to cTACE but achieves fewer procedures, less liver toxicity benefit, better tolerance, and shorter hospital stay.18,21,25-29 While another 2 studies in Asia

Table 8. Predicting Factors for CR of DEB-TACE Treatment in Patients With HCC.a

| Parameters                        | Univariate Logistic Regression | 95% CI | Multivariate Logistic Regression | 95% CI |
|----------------------------------|--------------------------------|--------|---------------------------------|--------|
|                                  | P Value | OR | Lower | Higher | P Value | OR | Lower | Higher |
| Age ≥ 60 years                   | .464    | 0.578 | 0.133 | 2.505  | -       | -   | -     | -     |
| Gender, Female                   | .924    | 0.917 | 0.153 | 5.508  | -       | -   | -     | -     |
| HBVb                             | .088    | 0.179 | 0.025 | 1.293  | -       | -   | -     | -     |
| Drink                            | .603    | 0.662 | 0.140 | 3.123  | -       | -   | -     | -     |
| Cirrhosis                        | .282    | 2.333 | 0.499 | 10.907 | -       | -   | -     | -     |
| Multifocal vs unifocal           | .968    | 0.971 | 0.222 | 4.243  | -       | -   | -     | -     |
| Largest nodule size ≥5.7 cm      | .208    | 0.371 | 0.079 | 1.738  | -       | -   | -     | -     |
| Bilobar vs unilobar              | .586    | 1.571 | 0.309 | 7.989  | -       | -   | -     | -     |
| Portal vein invasionc           | .117    | 0.172 | 0.019 | 1.551  | -       | -   | -     | -     |
| Hepatic vein invasionc           | -       | -     | -     | -     | -       | -   | -     | -     |
| Higher ECOGc                     | -       | -     | -     | -     | -       | -   | -     | -     |
| Higher Child-pugh stagec         | -       | -     | -     | -     | -       | -   | -     | -     |
| Higher BCLC stage                | .267    | 0.570 | 0.211 | 1.537  | -       | -   | -     | -     |
| WBC >4.80, 10^9 cell/L           | .846    | 1.154 | 0.272 | 4.895  | -       | -   | -     | -     |
| RBC >4.01, 10^{12} cell/L        | .726    | 1.300 | 0.300 | 5.637  | -       | -   | -     | -     |
| ANC%>64.10                      | .208    | 0.371 | 0.079 | 1.738  | -       | -   | -     | -     |
| HB >12.70, g/L                   | .478    | 1.750 | 0.373 | 8.201  | -       | -   | -     | -     |
| PLT >97.00, 10^9 cell/L          | .130    | 3.167 | 0.309 | 7.989  | -       | -   | -     | -     |
| ALB >37.20, g/L                  | .150    | 3.111 | 0.663 | 14.596 | -       | -   | -     | -     |
| TP >66.70, g/L                   | .464    | 1.731 | 0.399 | 7.505  | -       | -   | -     | -     |
| TBIL >17.10, μmol/L              | .264    | 0.431 | 0.099 | 1.886  | -       | -   | -     | -     |
| TBA >14.35, μL                   | .355    | 0.500 | 0.115 | 2.175  | -       | -   | -     | -     |
| ALT >31.00, μL                   | .464    | 0.578 | 0.133 | 2.505  | -       | -   | -     | -     |
| AST >40.0, μL                    | .025    | 0.139 | 0.025 | 0.785  | .073    | 0.089 | 0.006 | 1.251 |
| ALP >147.00, μL                  | .264    | 2.318 | 0.530 | 10.133 | -       | -   | -     | -     |
| BCr >66.00, μmol/L               | .208    | 2.692 | 0.575 | 12.596 | -       | -   | -     | -     |
| BUN >3.92, mmol/La                | .037    | 10.385 | 1.156 | 93.293 | -       | -   | -     | -     |
| AFP >18.46, μg/L                 | .968    | 0.971 | 0.222 | 4.243  | -       | -   | -     | -     |
| CEA >2.74, μg/Lb                 | -       | -     | -     | -     | -       | -   | -     | -     |
| CA199 >24.80, kU/L               | .038    | 0.162 | 0.029 | 0.908  | .041    | 0.066 | 0.005 | 0.891 |
| Previous cTACE                    | .654    | 1.407 | 0.316 | 6.265  | -       | -   | -     | -     |
| Previous Surgeryc                | -       | -     | -     | -     | -       | -   | -     | -     |
| Previous systematic chemotherapyc | -       | -     | -     | -     | -       | -   | -     | -     |
| Previous radiofrequency ablationc| -       | -     | -     | -     | -       | -   | -     | -     |
| Previous targeted therapyc       | -       | -     | -     | -     | -       | -   | -     | -     |
| Adriamycin drug(chemoembolization reagents)c | - | - | - | - | - | - | - | - |
| Irinotecan (Chemoembolization reagents) | .775  | 1.444 | 0.117 | 17.904 | -       | -   | -     | -     |
| Combination of ordinary embolization agent | .208  | 0.371 | 0.079 | 1.738  | -       | -   | -     | -     |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; AFP, alpha fetoprotein; ALP, alkaline phosphatase; ALB, albumin; ANC, absolute neutrophil count; BUN, blood urea nitrogen; BCLC, Barcelona Clinic Liver Cancer; BCr, blood creatinine; CEA, carcino-embryonic antigen; CA199, carbohydrate antigen199; cTACE, conventional transarterial chemo-embolization; ECOG, Eastern Cooperative Oncology Group; HB, hemoglobin; HCC, hepatocellular carcinoma; HBV, hepatic b virus; PLT, platelet; RBC, red blood cell; TP, total protein; TBIL, total bilirubin; TBA, total bile acid; WBC, white blood cell.

aData were presented as P value, OR (odds ratio), and 95% CI. Significance was determined by univariate and multivariate logistic regression analysis. All factors with P value < .1 in univariate model were further analyzed by multivariate model. P value < .05 was considered significant.

bDue to the high relevance among “HBV,” “AST,” “BUN,” and “CA199,” and lack of CR events or non-CR events, “HBV” and “BUN” were not available for multivariate logistic regression.

cDue to the lack of CR events or non-CR events, “hepatic vein invasion,” “higher ECOG,” “higher child-pugh stage,” “CEA >2.74 (μg/L),” “previous surgery,” “previous systematic chemotherapy,” “previous radiofrequency ablation,” “previous targeted therapy,” and “adriamycin drug(chemoembolization reagents)” were not available for univariate logistic model.

The boldface values stand for values with statistical significance.
inversely illuminate that DEB-TACE elevates treatment response, postpones the progression, and prolongs OS when compared to cTACE. The main cause of this controversy might result from the gap of technical ability between non-Asian physicians and Asian physicians in performing cTACE. Prior large-scale comparative studies on cTACE performed by experienced institutions mainly from Europe and/or America predominantly improved the outcomes of cTACE. As to our institution, DEB-TACE becomes a standardized procedure for patients with liver cancer not appropriate to receive curative therapies, and in the present study, CBs loaded with adriamycin or irinotecan were used for TACE treatment and achieved ORR as high as 83.7%, which is consistent with previous studies in which ORR of DEB-TACE ranged from 50% to 90%; 20.4% patients achieved CR, which is partially in line with previous studies with a CR of 17% to 68.7%.

Table 9. Predicting Factors for OS of DEB-TACE Treatment in Patients With HCC.\(^a\)

|                      | Univariate Cox Regression | 95% CI | Multivariate Cox Regression | 95% CI |
|----------------------|--------------------------|--------|----------------------------|--------|
|                      | \( P \) Value | HR   | Lower | Higher | \( P \) Value | HR   | Lower | Higher |
| Age ≥60 years        | .199          | 0.246 | 0.029 | 2.090   | -              | -    | -    | -     |
| Gender (Female)      | .815          | 0.776 | 0.092 | 6.506   | -              | -    | -    | -     |
| HBV                  | .251          | 0.244 | 0.022 | 2.711   | -              | -    | -    | -     |
| Drink                | .844          | 0.847 | 0.163 | 4.417   | -              | -    | -    | -     |
| Cirrhosis            | .381          | 0.511 | 0.149 | 2.295   | -              | -    | -    | -     |
| Multifocal vs unifocal| .451        | 2.304 | 0.264 | 20.145  | -              | -    | -    | -     |
| Largest nodule size ≥5.7 cm | .306   | 2.364 | 0.455 | 12.273  | -              | -    | -    | -     |
| Bilobar vs unilobar  | .301          | 2.226 | 0.489 | 10.141  | -              | -    | -    | -     |
| Portal vein invasion | .060          | 4.837 | 0.933 | 25.066  | .146          | 10.606| 0.440 | 255.690|
| Hepatic vein invasion| .601          | 0.566 | 0.067 | 4.777   | -              | -    | -    | -     |
| Higher ECOG          | .046          | 4.752 | 1.026 | 22.018  | .327          | 2.730 | 0.367 | 20.314|
| Higher child-pugh stage| .003      | 12.219| 2.334 | 63.984  | .159          | 13.138| 0.364 | 474.736|
| Higher BCLC stage    | .045          | 2.518 | 1.020 | 6.215   | .678          | 0.735 | 0.172 | 3.136 |
| WBC >4.80, \( \times 10^9 \) cell/L | .259   | 2.584 | 0.496 | 13.449  | -              | -    | -    | -     |
| RBC >4.01, \( \times 10^{12} \) cell/L | .474  | 0.560 | 0.115 | 2.736   | -              | -    | -    | -     |
| ANC% >64.10          | .139          | 3.463 | 0.667 | 17.988  | -              | -    | -    | -     |
| HB >12.70, g/L       | .529          | 0.615 | 0.135 | 2.796   | -              | -    | -    | -     |
| PLT >97.00, \( \times 10^9 \) cell/L | .821  | 1.189 | 0.265 | 5.331   | -              | -    | -    | -     |
| ALB >37.20, g/L      | .049          | 0.117 | 0.014 | 0.994   | .042          | 0.004 | 0.000 | 0.822 |
| TP >66.70, g/L       | .511          | 0.602 | 0.133 | 2.727   | -              | -    | -    | -     |
| TBIL >17.10, \( \mu \)mol/L | .202  | 5.574 | 0.117 | -       | -              | -    | -    | -     |
| TBA >14.35, I/L      | .146          | 0.295 | 0.057 | 1.527   | -              | -    | -    | -     |
| ALT >31.00, \( \mu \)L | .416      | 0.531 | 0.115 | 2.443   | -              | -    | -    | -     |
| AST >40.00, \( \mu \)L | .165      | 3.283 | 0.614 | 17.565  | -              | -    | -    | -     |
| ALP >147.00, \( \mu \)L | .370     | 1.987 | 0.443 | 8.920   | -              | -    | -    | -     |
| BCr >66.00, \( \mu \)mol/L | .476   | 0.542 | 0.101 | 2.913   | -              | -    | -    | -     |
| BUN >3.92, mmol/L    | .017          | 0.070 | 0.008 | 0.617   | .047          | 0.015 | 0.000 | 0.945 |
| AFP >18.46, \( \mu \)g/L | .579      | 0.652 | 0.144 | 2.954   | -              | -    | -    | -     |
| CEA >2.74, \( \mu \)g/L | .803      | 0.826 | 0.183 | 3.174   | -              | -    | -    | -     |
| CA199 >24.80, kU/L   | .180          | 3.083 | 0.595 | 15.986  | -              | -    | -    | -     |
| Previous cTACE       | .683          | 0.725 | 0.154 | 3.407   | -              | -    | -    | -     |
| Previous surgery     | .492          | 1.790 | 0.340 | 9.424   | -              | -    | -    | -     |
| Previous systematic chemotherapy | .207  | 4.099 | 0.458 | 36.729  | -              | -    | -    | -     |
| Previous radiofrequency ablation | .824 | 1.271 | 0.153 | 10.570  | -              | -    | -    | -     |
| Previous targeted therapy | .846       | 0.048 | -     | -       | -              | -    | -    | -     |
| Adriamycin drug (chemoembolization reagents) | .416  | 32.493 | -     | -       | -              | -    | -    | -     |
| Irinotecan (chemoembolization reagents) | .416  | 0.031 | -     | -       | -              | -    | -    | -     |
| Combination of ordinary embolization agent | .279  | 2.479 | 0.480 | 12.806  | -              | -    | -    | -     |

Abbreviations: ALT, alanine aminotransferase; ALB, albumin; ALP, alkaline phosphatase; ANC, absolute neutrophil count; AFP, alpha fetoprotein; AST, aspartate aminotransferase; BCLC, Barcelona Clinic Liver Cancer; BUN, blood urea nitrogen; CA199, carbohydrate antigen 199; cTACE, conventional transarterial chemo-embolization; CEA, carcino-embryonic antigen; ECOG, Eastern Cooperative Oncology Group; HCC, hepatocellular carcinoma; HBV, hepatitis B virus; HB, hemoglobin; PLT, platelet; RBC, red blood cell; TP, total protein; TBLI, total bilirubin; TBA, total bile acid; WBC, white blood cell. *Data were presented as \( P \) value, HR (hazard ratio), and 95% CI. Significance was determined by univariate and multivariate Cox regression analysis. All factors with \( P \) value < .1 in univariate model were further analyzed by multivariate model. \( P \) value < .05 was considered significant.
Table 10. Safety Profiles of DEB-TACE Treatment in Patients With HCC.

| Parameters                  | n (%)  |
|-----------------------------|--------|
| During DEB-TACE operation    |        |
| Pain                        | 17 (44.7) |
| Fever                       | 15 (39.5) |
| Nausea                      | 1 (2.6)  |
| Vomiting                    | 0 (0.0)  |
| Others                      | 1 (2.6)  |
| After DEB-TACE operation    |        |
| Pain                        | 23 (60.5) |
| Fever                       | 13 (34.2) |
| Nausea                      | 8 (21.1)  |
| Vomiting                    | 11 (28.9) |
| Liver dysfunction           | 21 (55.3) |
| Alopecia                    | 0 (0.0)  |
| Chromatosis                 | 2 (5.3)  |
| Bone marrow toxicity        | 4 (10.5)  |
| Others                      | 2 (5.3)  |

Abbreviation: DEB-TACE, drug-eluting beads transarterial chemoembolization.

*Data were presented as count (%).

embolization agent was used in our study due to economic conditions of the patients. Earlier studies have reported relatively good efficacy for DEB-TACE as well. In 2011, a prospective, randomized, and single-center study using DEB-TACE to treat patients with HCC reveals a CR rate of 51.5% and a PR rate of 48.5%. In another case–control study, the CR and PR rates of DEB-TACE are 35% and 50%, respectively. A pilot study elucidates that patients who were refractory to cTACE achieved a CR rate of 40% and a PR rate of 60%. Due to different patient eligibilities, sample sizes, or the criteria that is used to evaluate the clinical response, the CR and PR rates vary among studies. The light difference in the clinical outcomes among studies are mainly due to the diversified inclusion criteria of patients enrolled, for example, in the present study, we not only enrolled the patients with primary liver cancer having BCLC stages A, B, and C but also included patients with secondary liver cancer which would reduce the response rate. We also found that 1 patient was PD after treatment, and the possible reason might be that the patient was BCLC stage C, multifocal, bilobar, relapsed HCC case, and with portal vein invasion, which correlates with worse clinical response.

Additionally, CBs were used in the DEB-TACE procedure in our study, and a previous animal experiment reveals that CBs loaded with doxorubicin (CBDOX) could achieve a relatively high drug concentration in rabbits compared to lipiodol emulsion; meanwhile, CBDOX could also deliver the drug to a distance of 200 μm and lasted for at least 1 month, indicating a good efficacy of drug release of CBDOX. The efficacy of CBs has also been proved by other experiments in vitro, which displayed that CBs could provide controlled release of doxorubicin with the half-life period more than 2 months. In vivo, it is reported that the drug can be detected after 2 weeks in rabbits post the DEB-TACE by CBs.

Due to the diversified physical conditions, clinical properties, and biological features, the prognosis of patients with liver cancer receiving DEB-TACE treatment varies from each other. Thus, in order to better optimize the efficacy of DEB-TACE treatment and improve the prognosis of patients with liver cancer, it is essential to explore novel and convincing biomarkers for both clinical response and survival in patients by DEB-TACE treatment. A prospective historical cohort (mixed cohort design) study reveals that tumor size <5 cm and location in segments 1 or 4 correlates with higher possibility of CR in DEB-TACE-treated patients with HCC. In addition, another retrospective cohort study of DEB-TACE disclosed that tumor heterogeneity and tumor enhancement >50% predicts better CR but with a limited sample size (only 32 patients). Besides, a phase II trial illustrates that DEB-TACE achieves better objective response compared to cTACE in patients with HCC having Child-Pugh stage B, ECOG performance status 1, bilobar disease, or recurrent disease. In our study, we observed baseline high AST, high CA199, portal vein invasion, higher Child-pugh stage, and higher BCLC stage were associated with less possibility of clinical response by DEB-TACE treatment, while high BUN predicted a better clinical response achievement. Although the exact reason why these factors could predict clinical response was unclear, the possible explanation of the predictive value of these factors might be (1) AST was released to peripheral blood when hepatic cells are destroyed; thus in clinical practice, a high AST associates with a more severe liver function damage, meanwhile higher Child-pugh stage associates with worse liver function. CA199 has been used as a biomarker for diagnosing pancreatic cancer, rectal cancer, or liver cancer, and a higher CA199 might correlate with an advanced stage of cancer. Therefore, patients with baseline high AST and CA199 were less likely to achieve clinical response and might be explained by their worse liver function and more severe liver cancer. (2) Portal vein invasion and higher BCLC stage correlate with advanced liver cancer, which also suggest that those patients might not respond to DEB-TACE as good as patients with early-stage liver cancers. (3) Low BUN (divided as 3.92 mmol/L) correlated with more severe liver dysfunction, which reduced the response.

As for survival, a large sample size-based cohort study with 674 patients with HCC treated by DEB-TACE or cTACE presents that higher Child-pugh stage and portal vein invasion were independent predictors for worse OS. An randomized controlled trial study comparing DEB-TACE and cTACE found that higher ECOG stage and multiple tumors correlate with shorter OS independently in all patients with HCC. Another real-world setting study comparing DEB-TACE and cTACE disclosed that Bilobar and max diameter above 3.5 cm predicts lower OS. As to predictors for survival of DEB-TACE treatment alone, only a retrospective cohort study with limited patients (32 patients) reveals that tumor size above 6 cm is associated with worse OS. And a previous study in 2013 illuminates that high AFP, radiographically advanced HCC, high ECOG, high Child-pugh class, ascites, and high
Figure 1. OS analysis for subgroups by K-M curves. In DEB-TACE-treated patients with liver cancer, largest nodule size $\geq 5.7$ cm (A), portal vein invasion (C), higher ECOG performance status (D), higher Child-pugh stage (E), and high ALP (I) were associated with shorter OS; while high ALB (H) and high BUN (J) were correlated with favorable OS. No correlation was observed in unilobar versus bilobar (B), BCLC stage (F), and RBC level (G). ALP indicates alpha-fetoprotein; ALB, albumin; BUN, blood urea nitrogen; BCLC, Barcelona Clinic Liver Cancer; ECOG, Eastern Cooperative Oncology Group; RBC, red blood cells; OS, overall survival.
BUN are independently associated with worse survival, and the results are partly in accordance with ours. In this study, we disclosed that portal vein invasion, higher ECOG performance status, higher Child-pugh stage, and high ALP predict worse OS in DEB-TACE-treated patients, while high ALB and high BUN correlates with prolonged OS. ALB indicates albumin; BUN, blood urea nitrogen; BCLC, Barcelona Clinic Liver Cancer; DEB-TACE, drug-eluting beads transarterial chemoembolization; ECOG, Eastern Cooperative Oncology Group; HCC, hepatocellular carcinoma; OS, overall survival.

As to one of the most common adverse events of TACE, the occurrence rate of pain ranges from approximately 18.0% to 42.6% in patients treated with DEB-TACE, while in cTACE, the range roughly from 50.0% to 71.6%, suggesting DEB-TACE might be less painful compared to cTACE. This is the first study that analyzed the comprehensive factors affecting clinical response and survival in patients with liver cancer using DEB-TACE treatment, including demographic features, medical histories, clinicopathological properties, biochemical indexes, previous treatments, chemoembolization reagents. However, there were some limitations in this study. First, the relatively small size sample with 49 patients limited the analysis of some key factors in univariate regression analysis due to the lack of effective events as well as multivariate were not available for ORR prediction due to too many variables compared to small sample population enrolled. Second, the follow-up period was short, and the predictive value of the factors for long-term survival was not analyzed. Thus, further studies with larger sample size and longer follow-up duration are needed in the future.

In conclusion, this study observed that DEB-TACE was effective and well tolerated for patients with liver cancer, and...
high AST, high ALP, low ALB, low BUN, portal vein invasion, higher Child-pugh stage, higher BCLC stage, higher ECOG performance status were correlated with worse outcomes.

Declaration of Conflicting Interests
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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