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ORIGINAL ARTICLE

Drug-eluting bead transarterial chemoembolization for hepatocellular carcinoma: does size really matter?

Sieh-Yang Lee
Hsin-You Ou
Chun-Yen Yu
Tung-Liang Huang
Leo Leung-Chit Tsang
Yu-Fan Cheng

PURPOSE
We aimed to compare the safety and effectiveness of 100–300 μm versus 300–500 μm drug-eluting bead transarterial chemoembolization (DEB-TACE) and to investigate the impact of tumor and feeding artery size on treatment outcome of different particle sizes in the treatment of hepatocellular carcinoma (HCC).

METHODS
This retrospective cohort study enrolled 234 consecutive patients who underwent TACE using 100–300 μm DEB (Group A, n=75) and 300–500 μm DEB (Group B, n=159) in a tertiary center between August 2012 and March 2017. Initial treatment response and adverse events were assessed using modified Response Evaluation Criteria in Solid Tumors (mRECIST) and National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, respectively.

RESULTS
A total of 704 HCCs in 234 patients were evaluated. The average index tumor size was 3.8 cm. Multivariate analysis showed that tumor size, lobe involvement, particle size, and tumor location were significant predictive factors of complete response. The overall rate of complete response in groups A and B were 56.0% and 33.3% ($P = 0.001$), respectively. Group A had higher complete response rate than group B in the subgroup of BCLC B with tumor <3 cm (57.9% vs. 21.1%; $P = 0.020$) and subgroup of feeding artery ≥0.9 mm (55.2% vs. 30.9%; $P = 0.014$). There were fewer major complications in group A compared with group B (0% vs. 6.9%, $P = 0.018$).

CONCLUSION
TACE with 100–300 μm DEB is associated with better initial treatment response and fewer major complications compared with 300–500 μm. Our study also highlights the impact of tumor characteristics on treatment outcome of different DEB size, which might help to select the optimal sphere size for TACE in the treatment of HCC.

Transarterial chemoembolization (TACE) is an established standard of treatment for nonsurgical patients with Barcelona Clinic Liver Cancer (BCLC) intermediate stage hepatocellular carcinoma (HCC) and preserved liver function (1). The optimal TACE should allow maximal chemotherapeutic drug sustained within the target tumor and optimal occlusion of tumor feeding vessel as well as minimal systemic side effects. Drug-eluting bead TACE (DEB-TACE) has been developed to provide sustained drug delivery locally, combined with ischemic response of the liver tumor (2). In clinical practice, there are different sizes of DEB particles available for use. The published literature reported variable treatment outcomes with different DEB particle sizes (3–7). Although previous studies showed promising results with small DEB particles over their large counterparts, the influence of patient and tumor characteristics on treatment outcomes of different DEB particle size are yet to be fully elucidated. Recent studies have suggested that sizes of the tumor and feeding artery were significant predictors of treatment response and histological tumor necrosis (8, 9). Therefore, considering the effect of tumor size and feeding artery, the optimal DEB particle size for any given hepatic tumor remains to be determined.

The present study aimed to compare the safety and effectiveness of 100–300 μm versus 300–500 μm DEB-TACE in patients with HCC. Particularly, treatment response be-

From the Department of Diagnostic Radiology (Y.F.C. ✉ *prof.chengyufan@gmail.com*), Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taiwan.

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tween the two groups was compared according to size of index tumor and feeding vessel.

Methods

Patient selection

This retrospective study was approved by the local ethics committee (protocol number: 201701554B0). Written informed consent was obtained from all patients before treatment. Between August 2012 and March 2017, 248 consecutive treatment-naïve patients who underwent DEB-TACE in a single tertiary center were reviewed. Each decision to treat was determined in consensus by a multidisciplinary board of a hepatologist, oncologist, liver transplant surgeon, and interventional radiologist. The inclusion criteria were as follows: *(i)* HCC diagnosed by pathology or noninvasive criteria based on the American Association for the Study of the Liver Disease (AASLD) guidelines (1), *(ii)* TACE procedure with 100–300 µm/ 300–500 µm drug-eluting beads, *(iii)* Child-Pugh class A/B/C disease, *(iv)* no combination treatment with other therapy, and *(v)* availability of computed tomography (CT) and/or magnetic resonance imaging (MRI) and serum data. A total of 14 patients were excluded for the following reasons: HCCs treated by 70–150 µm/ 500–700 µm DEB (n=11), combination treatment with other therapy (n=2), and secondary malignancy (n=1). Finally, a total of 234 patients were analyzed. Seventy-five patients treated by small (100–300 µm) DEB were designated as group A and 159 patients treated by large (300–500 µm) DEB were designated as group B. During the study period, 300–500 µm beads were used early for TACE, while 100–300 µm beads were chosen later.

Main points

- Drug-eluting bead transarterial chemoembolization (DEB-TACE) with 100–300 µm beads is associated with better treatment response and fewer major complications compared with 300–500 µm beads.
- DEB size and tumor characteristics including tumor size, lobe involvement, and tumor location are significant predictive factors of complete response.
- Tumor size and feeding artery size are useful parameters to differentiate treatment outcome between large and small DEB, particularly in patients with BCLC B, tumor size <3 cm and feeding artery size ≥0.9 mm.

DEB TACE procedure

After common femoral artery cannulation under local anesthesia, each first-time procedure was started with digital subtraction angiography (DSA) of celiac and superior mesenteric artery with a 4.0 F catheter (Optitorque, Terumo) adapted to arterial anatomy variations. The segmental or subsegmental feeding arteries supplying HCC were catheterized with a 2.7 F coaxial microcatheter (Progreat, Terumo) with adapted microwire. Then, embolization of hypervascular lesions was performed with a slow fluoroscopy-guided injection of iodinated contrast material mixed with 100–300 µm or 500–700 µm DC-Beads (Biocompatibles) impregnated with 50 mg of doxorubicin in each vial. The amount of DC-Bead was adapted to achieve near stasis of blood flow of the feeding artery without exceeding two vials. If embolization endpoint was not achieved after injection of the scheduled volume of loaded beads, Gelfoam (gelatin sponge) was administered until near stasis of the target lesion had been reached. Follow-up DSA was performed from the common hepatic artery to confirm no residual tumor enhancement.

Imaging techniques

Multiphasic helical CT was performed with a 128-MDCT scanner. MRI scan was carried out using a 1.5 T scanner. Precontrast and postcontrast dynamic images were obtained for both CT and MRI images. For MRI, series of T2-weighted, in- and out-of-phase T1-weighted, and diffusion-weighted images were collected using a 3D-gradient echo sequence.

Review of initial images and assessment of therapeutic effects

All patients underwent imaging examination and blood sampling within 1 month of treatment. Two experienced radiologists who were blinded to patients and DEB particle size retrospectively reviewed the CT/MRI images and angiographic studies of all patients before and after DEB-TACE. The division of the liver was delineated according to the Couinaud's classification. Segments 5, 6, 7, and 8 were designated as the right liver, while segments 2 and 3 were designated as the left liver. If the tumor involved wholly or partly in segment 4 or 1, it was considered as the median liver. Distance to liver capsule was reported peripheral if the liver tumor margin was within 1 cm from the liver capsule. For angiographic studies, the diameter of the largest feeding vessel of liver tumor was designated as smaller than the diameter of a microcatheter (<0.9 mm) or as equal to or larger than the diameter of a microcatheter (≥0.9 mm).

After DEB-TACE, the therapeutic effects were assessed by comparing the preprocedural CT images to the 1-month postprocedural images. Tumor changes were evaluated on postcontrast CT or MRI based on mRECIST criteria (10). If a patient had multiple tumors, the treatment response was evaluated with overall tumor response, which included combined evaluation of target lesions, nontarget lesions, and new lesions. Tumor response to treatment were classified as complete response (CR), partial response (PR), progressive disease, and stable disease. Objective response rate (ORR) was defined as the summation of CR and PR. Complications after treatment were documented using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE version 5.0) (11): grade 1, mild or asymptomatic adverse events; grade 2, moderate adverse events requiring minimal, local, and noninvasive intervention; grade 3, severe or disabling adverse events with prolonged hospitalization indicated; grade 4, life-threatening adverse events requiring urgent intervention; and grade 5, death related to adverse events.

Statistical analysis

All statistical analyses were conducted using SPSS software (version 22; SPSS, IBM Corp.). Comparison of continuous variables between the groups was performed for statistical significance using Student's t-test (or Mann-Whitney U test, if appropriate) and categorical variables were examined using chi-square test (or Fisher's exact test, if appropriate). Logistic regression was conducted for univariate and multivariate analysis with the odds ratio (OR) and confidence interval (CI) calculated. A multivariate logistic model was built, and stepwise method was adopted to identify the best subset of predictors. All variables in univariate analysis were included in the multivariate regression model. Goodness of fit of the regression models was evaluated by using the Hosmer–Lemeshow test. All data were reported as the mean ± standard deviation (SD) or number (%) as appropriate. The *P* value for statistical significance was set at <0.05.

Results

A total of 704 HCCs in 234 patients were evaluated for treatment response and the average index tumor size was 3.8 cm. In the study population, the patients were primarily men (79.1%) and the median age was 62 years (range, 31–90 years). Cirrhosis was present in 227 patients (97%), and hepatitis B (50.9%) was the most common underlying disease. Most patients were in Child-Pugh class A (85.5%) and in BCLC stage B (41.0%). There were 75 patients (32.0%) in group A and 159 patients (68.0%) in group B. The baseline differences between patients in group A and group B are listed in Table 1. Group A and group B had similar ages (P = 0.47), sex (P = 0.81), Child-Pugh class (P = 0.77) and underlying disease (P = 0.77). The mean size of the index tumor was smaller in group A than group B (2.8 vs. 4.3 cm; P < 0.001). There were no significant differences in the percentage of portal vein thrombosis, tumor location, and multiplicity of the tumor between the two groups.

The overall CR and ORR were significantly different between group A and group B (CR: 56.0% vs. 33.3%, P < 0.001; ORR: 78.7% vs. 60.4%, P = 0.006) (Table 2). In substratification analysis of patients according to BCLC stage, group A had higher CR and ORR in BCLC-B (CR: 50.0% vs. 22.1%, P = 0.007; ORR: 78.6% vs. 55.9%, P = 0.037), and higher CR in BCLC-C (80.0% vs. 22.6%; P = 0.010) compared with group B. When patients were stratified based on the largest feeding artery size, CR and ORR were higher in group A than group B (CR: 55.2% vs. 30.9%, P = 0.014; ORR: 86.2% vs. 61.8%, P = 0.012) in the subgroup of feeding artery ≥0.9 mm. Multivariate analysis demonstrated that small tumor size (<5 cm) (OR= 2.75; 95% CI, 1.26–6.03; P = 0.011), unilobar involvement (OR= 2.04; 95% CI, 1.11–3.76; P = 0.022), 100–300 µm DEB (OR= 1.96; 95% CI, 1.06–3.60; P = 0.031), and tumor located in the right liver (versus median liver) (OR= 2.30; 95% CI, 1.21–4.37; P = 0.011) were significant predictors of CR (Table 3). Hosmer and Lemeshow goodness-of-fit test was not significant (P = 0.49), which was indicative of good model fit to the data.

Small tumor size (<5 cm) was strongly associated with CR compared with ≥5 cm tumor (46.6% vs. 19.6%, P < 0.001) (Fig.). After subclassifying patients with BCLC stage A and BCLC stage B by index tumor size, group A had higher CR than group B in the subgroup of BCLC B with tumor <3

Table 1. Demographic and clinical data of HCC patients in Group A and Group B

Parameters	Group A (100–300 µm) n=75	Group B (300–500 µm) n=159	*P*
Age at diagnosis (years), mean±SD	62.45±10.7	61.3±11.8	0.47
Sex (male/female)	60/15	125/34	0.81
Underlying disease			0.77
HBV	39 (52.0)	80 (50.3)	
HCV	21 (28.0)	48 (30.2)	
HBV and HCV	4 (5.3)	13 (8.2)	
Others	11 (14.7)	18 (11.3)	
Cirrhosis	75 (100.0)	152 (95.6)	0.53
Child-Pugh class			0.77
A	65 (86.7)	128 (80.5)	
B	10 (13.3)	23 (14.5)	
C	0 (0)	1 (0.6)	
BCLC stage			0.037
0	4 (5.3)	8 (5.0)	
A	37 (49.3)	50 (31.4)	
B	28 (37.3)	68 (42.8)	
C	5 (6.7)	31 (19.5)	
D	1 (1.3)	2 (1.3)	
Tumor burden			
Tumor size (cm), mean±SD	2.8±1.6	4.3±2.3	<0.001
Single/multiple	19 (25.3) /56 (74.7)	47 (29.6) /112 (70.4)	0.50
Unilobar/bilobar	52 (69.3) /23 (30.7)	93 (58.5) /66 (41.5)	0.11
Portal vein thrombosis	2 (2.7)	13 (8.2)	0.11
Imaging response			0.005
Complete responses	42 (56.0)	53 (33.3)	
Partial responses	17 (22.7)	43 (27.0)	
Stable disease	9 (12.0)	45 (28.3)	
Progressive disease	7 (9.3)	18 (11.3)	

Data are presented as n (%).
HCC, hepatocellular carcinoma; SD, standard deviation; HBV, hepatitis B virus; HCV, hepatitis C virus; BCLC, Barcelona Clinic Liver Cancer.

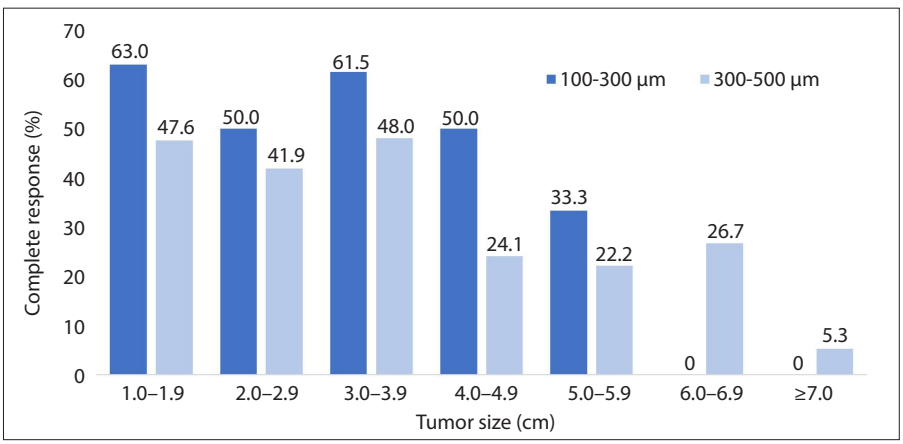

Figure. Complete response according to index tumor size. Small tumor size (<5 cm) was strongly associated with complete response compared with ≥5 cm tumor (46.6% vs. 19.6%, P < 0.001).

Table 2. Imaging response between Group A and Group B according to size of index tumor and feeding artery

	CR			ORR		
Variables	Group A	Group B	*P*	Group A	Group B	*P*
Overall	42/75 (56.0)	53/159 (33.3)	<0.001	59/75 (78.7)	96/159 (60.4)	0.006
Tumor size						
BCLC A	n=37	n=50		n=37	n=50	
Overall	19/37 (51.4)	25/50 (50.0)	0.90	28/37 (75.7)	37/50 (74.0)	0.86
≤ 2 cm	6/12 (50.0)	9/12 (75.0)	0.21	7/12 (58.3)	9/12 (75.0)	0.39
> 2 cm	13/25 (52.0)	16/38 (42.1)	0.44	21/25 (84.0)	28/38 (73.7)	0.34
BCLC B	n=28	n=68		n=28	n=68	
Overall	14/28 (50.0)	15/68 (22.1)	0.007	22/28 (78.6)	38/68 (55.9)	0.037
<3 cm	11/19 (57.9)	4/19 (21.1)	0.020	15/19 (78.9)	9/19 (47.4)	0.044
3–5 cm	3/7 (42.9)	6/24 (25.0)	0.36	6/7 (85.7)	16/24 (66.7)	0.33
>5 cm	0/2 (2)	5/25 (20.0)	0.48	1/2 (50.0)	13/25 (52.0)	0.96
BCLC C	n=5	n=31		n=5	n=31	
Overall	4/5 (80.0)	7/31 (22.6)	0.010	4/5 (80.0)	12/31 (38.7)	0.085
Feeding artery						
<0.9 mm	26/46 (56.5)	14/36 (38.9)	0.11	34/46 (73.9)	20/36 (55.6)	0.082
≥0.9 mm	16/29 (55.2)	38/123 (30.9)	0.014	25/29 (86.2)	76/123 (61.8)	0.012

Data are presented as n/N (%).
CR, complete response; ORR, objective response rates; BCLC, Barcelona Clinic Liver Cancer.

cm (57.9% vs. 21.1%; $P = 0.020$). There were no significant differences in CR and ORR between the two groups in the subgroup of BCLC A (≤2 cm and >2 cm) and BCLC B (3–5 cm and >5 cm) (Table 3).

As listed in Table 4, CTCAE grade III adverse events were more prevalent in group B compared with group A (6.9% vs. 0%, $P = 0.018$). Group A had similar CTCAE grade I/II adverse events with group B (44.0% vs. 40.3%, $P = 0.67$). There were no significant differences between the groups according to the BCLC stage and tumor size as well as feeding artery size.

Discussion

In the current study, we found that DEB-TACE with 100–300 μm beads had a superior initial radiological response and less major complications compared with 300–500 μm beads in patients with HCC. In particular, DEB-TACE with 100–300 μm beads was more effective in patients with BCLC stage B and small tumor (<3 cm), and large feeding artery (≥0.9 mm). Moreover, tumor characteristics and particle size were independent predictors of CR. These results suggested that the impact of tumor and feeding artery size should be taken into consideration in selecting the optimal particle size for DEB-TACE.

DEB-TACE has been proven to provide at least similar treatment response and fewer complications than cTACE (6, 12). However, there is no current consensus on optimal particle size to use in DEB-TACE. Our study showed that 100–300 μm beads resulted in better treatment response than 300–500 μm beads, which was consistent with the previous studies (7). The higher survival and radiological response of small-sized DEB might be attributed to increased surface area and more distal distribution of the smaller beads. With smaller particle size, the surface area of DEB was increased substantially, causing a greater release of the chemotherapeutic agent within the tumor. This theory was supported by a pharmacokinetic study in pigs (13) which revealed significantly higher plasma level of doxorubicin and larger areas of tumor necrosis with 100–300 μm beads compared with 700–900 μm beads. Furthermore, Lee et al. (14) demonstrated deeper penetration of smaller beads into the intratumoral vascular bed by MRI in rabbits with VX2 liver tumors. In the evaluation after arterial embolization, 100–300 μm beads were detected at the rim and inside the tumor whereas 300–500 μm beads were distributed outside the tumor. The ability to deposit in the distal vessels of small particles may promote more localized chemotherapeutic effect, leading to larger areas of tumor necrosis.

BCLC intermediate stage includes a heterogeneous patient population with varying tumor characteristics and liver function, which poses serious challenges for therapeutic management (15). Although previous studies of DEB-TACE revealed the superiority of smaller particle on treatment outcome over its larger counterparts (7), the influence of tumor size and BCLC stage on clinical results has yet to be discussed. The present study demonstrated that 100–300 μm beads provided better radiological response than 300–500 μm beads in patients with BCLC B and tumor size <3 cm. These findings might be explained by the intratumoral and peritumoral distribution of the small DEB and distance of microsatellites from the main tumor, which is positively correlated with the tumor size. Previous studies reported variable distance between the microsatellite and main tumor depending on the size and histologic grading of the liver tumor (16–18). With 100–300 μm beads, the particles were detected at a mean distance of 4.9 mm from the tumor margin (19), which is where microsatellites are likely to be in HCCs <5 cm. In our study, the tumoricidal effect of small particles could also be observed in patients with HCC of 3–5 cm, which showed a trend toward better imaging response albeit statistically insignificant.

Moreover, our study showed that 100–300 μm beads had higher CR and ORR than 300–500 μm beads in a tumor having the largest feeding artery with a diameter equal to or wider than 0.9 mm. Although the exact mechanism remains unclear, it is possible to propose an explanation based on the understandings of HCC pathogenesis. During hepatocarcinogenesis, HCC tumors may receive blood flow from hepatic arteries and portal veins (20). In general, tumors receiving more portal blood flow have less well-developed feeding arteries and vice versa. When the largest feeding artery size is under the size threshold, these tumors preserve enough portal blood flow that diminishes the antitumor activity of the transarterially delivered DEB. In contrast, when the dominant blood supply transitions from portal veins to hepatic arteries, 100–300 μm beads can penetrate deeper into the intratumoral

Table 3. Univariate and multivariate analysis to identify prognostic factors for complete response

	Univariate analysis			Multivariate analysis		
Variables	OR	95% CI	*P*	OR	95% CI	*P*
Sex						
Male	1.90	0.96–3.78	0.065			
Female	Reference					
Underlying disease						
HBV	1.74	0.75–4.07	0.20			
HCV	0.77	0.31–1.96	0.59			
HBV and HCV	1.33	0.39–4.56	0.65			
Others	Reference					
Cirrhosis						
Yes	1.70	0.32–8.97	0.53			
No	Reference					
Tumor location						
Right liver	2.44	1.34–4.43	0.003	2.30	1.21–4.37	0.011
Left liver	1.12	0.44–2.80	0.075	0.79	0.37–2.59	0.96
Median liver	Reference					
Lobe involvement						
Unilobar	2.53	1.43–4.47	0.001	2.04	1.11–3.76	0.022
Bilobar	Reference					
Portal vein thrombosis						
No	10.33	1.34–79.98	0.025	8.23	0.98–68.99	0.052
Yes	Reference					
Index tumor size (cm)						
<5cm	3.57	1.74–7.36	0.001	2.75	1.26–6.03	0.011
≥5 cm	Reference					
DEB particle size (μm)						
100–300	2.62	1.49–4.60	<0.001	1.96	1.06–3.60	0.031
300–500	Reference					
Feeding artery (mm)						
<0.9	1.73	1.00–2.98	0.049			
≥0.9	Reference					
Peripheral location						
Yes	0.65	0.33–1.26	0.20			
No	Reference					
Nodularity						
Single	1.48	0.83–2.63	0.19			
Multiple	Reference					

Data are presented as n (%).
OR, odds ratio; CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; DEB, drug-eluting beads.

and peritumoral vascular beds whereas 300–500 μm beads only block proximal arterial branch. Taken together, these findings suggest that the size of the index tumor and feeding artery might affect treatment response and should be taken into consideration when selecting the optimal DEB particle size for TACE.

Compared with 100–300 μm beads, the present study revealed a significantly higher incidence of major adverse events after DEB-TACE with 300–500 μm beads. In theory, larger DEBs tend to have peritumoral distribution and block proximal feeding artery, leading to more global ischemia and increased risk of nontarget embolization of normal liver parenchyma. Accordingly, in our study, the complication related to ischemic damage of the nontumoral liver parenchyma after TACE with larger DEB were higher than their smaller counterparts because of a higher embolic effect of the larger particles on normal parenchyma. These results suggested that small-sized DEB might be preferable to large-sized DEB in patients with impaired liver function.

There were several limitations to our study. First, our results might be affected by the inherent bias of retrospectively designed study. Despite similar demographic characteristics and clinical data, there were significant differences in the tumor size and BCLC stage between the two groups. Thus, subgroup analysis of treatment response according to tumor size and BCLC stage was conducted to reduce the effect of these confounding factors. Second, 100–300 μm beads were not available for use at our institution during the early study period. The 300–500 μm beads were chosen for TACE early on, while 100–300 μm beads were used later. Although the operators were experienced interventional radiologists, refinement of the embolization techniques of the operators with increasing TACE experience over time might be a potential confounding factor. Third, the present study included patients who received multimodality treatment for downstaging/bridging therapies and liver transplantation after initial TACE. The long-term outcomes might not be representative of the treatment effect of TACE, which may be profoundly influenced by multimodality treatment. This study assessed initial treatment response to TACE, which was demonstrated to be a robust predictor of favorable overall and tumor-free survival in HCC patients (21–23).

In conclusion, DEB-TACE with 100–300 μm beads is associated with better treatment response and fewer major complications compared with 300–500 μm beads. Tumor size and feeding artery size are useful parameters to differentiate treatment outcome between large and small DEB, particularly in patients with BCLC B and tumor size <3 cm and feeding artery size ≥0.9 mm. Our findings highlight the impact of tumor characteristics on treatment outcome of different DEB size, which might help to select the optimal sphere size for TACE in the treatment of HCC.

Table 4. Comparison of adverse events related to DEB-TACE between Group A and Group B

Variables	Group A (300–500 μm) n=75	Group B (300–500 μm) n=159	*P*
Grade I and II	33 (44.0)	64 (40.3)	0.67
Abdominal pain	23 (30.7)	44 (27.7)	
Fever	12 (16.0)	31 (31.0)	
Nausea with vomiting	2 (2.7)	4 (2.5)	
Grade III	0 (0)	11 (6.9)	0.018
ALT elevation (≥ Grade III)	0 (0)	5 (3.1)	
Severe abdominal pain with prolonged hospitalization	0 (0)	4 (2.5)	
Bradycardia	0 (0)	1 (0.6)	
Encephalopathy	0 (0)	1 (0.6)	
BCLC stage A			
Overall	14/37 (37.8)	17/50 (34.0)	0.71
≤2 cm	2/12 (16.7)	3/12 (25.0)	0.62
>2 cm	12/25 (48.0)	14/38 (36.8)	0.38
BCLC stage B			
Overall	16/28 (57.1)	35/68 (51.5)	0.61
<3 cm	12/19 (63.2)	9/19 (47.4)	0.33
3–5 cm	3/7 (42.9)	11/24 (45.8)	0.89
>5 cm	1/2 (50.0)	15/25 (60.0)	0.78
BCLC C			
Overall	1/5 (20.0)	16/31 (51.6)	0.19
Feeding artery (mm)			
<0.9	20/46 (43.5)	16/36 (38.9)	0.68
≥0.9	13/29 (44.8)	61/123 (49.6)	0.64

Data are presented as n/N (%).
DEB-TACE, drug-eluting bead transarterial chemoembolization; ALT, alanine aminotransferase; BCLC, Barcelona Clinic Liver Cancer.

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Conflict of interest disclosure

The authors declared no conflicts of interest.

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