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Comprehensive analysis of common safety profiles and their predictive factors in 520 records of liver cancer patients treated by drug-eluting beads transarterial chemoembolization

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Abstract

This study aimed to investigate the difference of common adverse events (AEs) between patients experienced first drug-eluting beads transarterial chemoembolization (DEB-TACE; FD) and second or higher DEB-TACE (SHD), and the factors influencing AEs.

Five hundred twenty DEB-TACE records were retrospectively reviewed in this cohort study, among which 284 and 236 records were in FD and SHD groups, respectively. The incidence and/or severity of pain, fever, vomiting, and increased blood pressure (BP) were collected.

Pain numerical rating scale (NRS) score, pain severity, body temperature, fever severity, and fever lasting days were higher in FD group than in SHD group, while no difference of vomiting and increased BP between 2 groups were disclosed. Age ≥65 years was associated with decreased high fever and less possibility of vomiting in FD group, and lower pain and fever severity in SHD group; Male decreased the possibility of vomiting in both the groups, and reduced increased BP incidence in SHD group; diabetes history correlated with decreased pain degree and less fever in FD group.

In conclusion, SHD was better tolerated compared with FD in liver cancer patients, and older age as well as male were correlated with less occurrence or severity of common AEs in DEB-TACE operation.

Abbreviations: AEs = adverse events, BCLC = Barcelona Clinic Liver Cancer, BP = blood pressure, CCA = cholangiocarcinoma, cTACE = conventional TACE, DEB-TACE = drug-eluting beads transarterial chemoembolization, FD = first DEB-TACE, HCC = hepatocellular cancer, MDT = multidisciplinary teamwork, NRS = numerical rating scale, OS = overall survival, SE = standard error, SHD = second or higher DEB-TACE, TACE = transarterial chemoembolization.

Keywords: adverse events (AEs), drug-eluting beads transarterial chemoembolization (DEB-TACE), fever, increased blood pressure, liver cancer, pain, vomiting

1. Introduction

Liver cancer, as one of the malignant tumors and the second leading cause of cancer deaths of men in less developed countries, consists of hepatocellular cancer (HCC), cholangiocarcinoma (CCA), and mixed hepatocarcinoma.[1,2] Epidemiologic survey displays that HCC is the main form of liver cancer, accounting for 70% to 90% liver cancers, followed by CCA with the proportion of 10%.[3,4] As to treatment for patients with middle staged liver cancer who are inappropriate candidates for curative therapies,

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transarterial chemoembolization (TACE) is regarded as one of the standard choices according to the Barcelona Clinic Liver Cancer (BCLC) classification.[4,5]

Drug-eluting beads TACE (DEB-TACE), a new technique for chemoembolization using microbeads with diameter ranging from 100 to 900 μm, ensures more sustained drug delivery and permanent vascular embolization.[6] Although this approach has not been demonstrated to be superior to conventional TACE (cTACE), less chemotherapy-associated toxicity occurs in DEB-TACE treatment because of the lower systemic exposure to chemotherapeutics, and a recent Asian study shows DEB-TACE achieves an increased overall survival (OS) compared with cTACE.[7–9] Like every invasive treatment, DEB-TACE bears the risk of side effects, among which abdominal pain, fever, vomiting, and increased blood pressure are the most common adverse events (AEs).[10–13] However, few studies with a large sample size exploring the correlation of treatment cycles with incidence of AEs and the comprehensive factors affecting AEs to DEB-TACE treatment have been performed. Therefore, this study reviewed 520 records of DEB-TACE treatment and aimed to investigate the difference of common AEs between patients who experienced first DEB-TACE (FD) and patients who experienced second or higher DEB-TACE (SHD), and further explore the factors influencing AEs.

2. Materials and methods

2.1. Patients

Five hundred twenty records of DEB-TACE treatment in 408 liver cancer patients, in The First Affiliated Hospital, College of Medicine, Zhejiang University, between October 2015 and April 2017, were retrospective reviewed in this cohort study. The inclusion criteria were as follows: patients were diagnosed with primary liver cancer, including HCC, CCA, and mixed hepatocarcinoma or with secondary liver cancer, which were confirmed by pathological findings, clinical assessments, and radiographic examinations; underwent DEB-TACE treatment; and completed data of common AEs, including pain, fever, vomiting, and increased blood pressure within 3 days postoperation.

2.2. Ethic statement

Written informed consents or oral agreements (telephone with recording) were obtained from all patients. The study was approved by the Ethical Committee of The First Affiliated Hospital, College of Medicine, Zhejiang University, and carried out strictly according to the Declaration of Helsinki.

2.3. DEB-TACE procedure

DEB-TACE was performed on all patients on demand, which was determined by the assessment of multidisciplinary teamwork (MDT). CalliSpheres Beads (Jiangsu Hengrui Medicine Co. Ltd., Jiangsu, China) with the diameter ranging from 100 to 300 μm were used as carriers in each procedure. The beads were loaded with adriamycin drug (Adriamycin, Pirarubicin, or Epirubicin) at the concentration of 50 to 100 mg; the mean dose was 60 mg for patients with primary liver cancer. For patients with secondary liver cancer, the beads were loaded with Irinotecan at the concentration of 100 mg.

The loading process was performed as follows: chemoembolization reagents were dissolved to solution at the concentration of 20 mg/mL; the supernatant was extracted after 1 vial of CalliSpheres beads was shaken up; then, the remaining part, which mainly includes beads, and the chemoembolization solution were mixed by a tee joint; and then the mixed solution was shook up and stand for 30 minutes at room temperature of 23°C to 28°C; subsequently, the nonionic contrast agent was added and the mixed solution was stood for another 5 minutes for further application.

The DEB-TACE procedure was carried out under local anesthesia. Hepatic angiography was conducted to detect the tumor supplying vessels and 2.4 French microcatheter (Merit Maestro; Merit Medical System, Inc., UT) was used for the embolization of tumor supplying vessel. The mixed solution of CalliSpheres Beads and chemoembolization reagents was injected at the rate of 1 mL/min, and the chemoembolization 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 blushed tumor still existed. If there were still blushed tumors existed when a bottle of CalliSpheres Bead was emptied, the embolization was continued until there were no more blushed tumors. Post-operation, the microcatheter was pulled out and hemostasis by compression was performed, and the wound was bound up for 12 hours.

2.4. Treatment post DEB-TACE

Patients with postoperative nausea and vomiting were treated with an intravenously injection of tropisetron or ondansetron. Pethidine, dexamethasone, and lidocaine were given as analgesic treatment for pain. In addition, patients with infection were treated with sulperazone 2 g/q12 h and levofloxacin 500 mg/q24 h.

2.5. Data collection, assessments, and definitions

Characteristics of patients before DEB-TACE treatment were collected from Hospital Electronic Database, including age, gender, diagnosis, medical history or complications (hepatic B, liver cirrhosis, hypertension, diabetes mellitus, cardiovascular and cerebrovascular diseases, other tumor history, and liver cancer surgery or transplantation), and cycles of DEB-TACE.

The assessments of common AEs were obtained, including pain incidence, numerical rating scale (NRS) of pain, severity grade, and times of pain; body temperature, fever incidence, fever severity, fever lasting days; incidence of vomiting and increased blood pressure. The severity grade of pain was defined as[3] no pain: pain NRS score 0; mild pain: pain NRS score 1 to 3; moderate pain: pain NRS score 4 to 6; and severe pain: pain NRS score 7 to 10. The fever severity grade was evaluated as no fever: body temperature between 36.0°C and 37.2°C; low fever: body temperature between 37.3°C and 38.0°C; moderate fever: body temperature between 38.1°C and 39.0°C; high fever: body temperature between 39.1°C and 41.0°C; and extremely high fever: body temperature above 41.0°C.

2.6. Statistics

Statistical analysis was performed using SPSS 22.0 software (IBM, Armonk, New York) and Graphpad Prism 5.01 software (GraphPad Software Inc, La Jolla, CA). Data were presented as count (percentage) and mean ± standard error (SE). Comparison between/among groups was determined by t test or Chi-square test. $P < .05$ was considered significant.

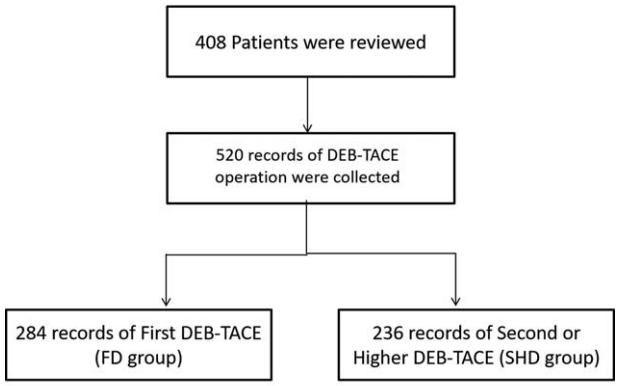

Figure 1. Study flow.

3. Results

3.1. Study flow

Four hundred eight liver cancer patients were included and 520 records of DEB-TACE operation were analyzed in this study. As to cycles of DEB-TACE treatment, there were 284 records of first DEB-TACE and 236 records of second or higher DEB-TACE, which were defined as FD group and SHD group, respectively (Fig. 1).

3.2. Baseline characteristics

As presented in Table 1, 92 (32.4%) cases were ≥65 years of age with 230 males (81.0%) in FD group, while 77 (32.6%) cases were ≥65 years of age with 195 males (82.0%) in SHD group. No difference of age and gender between 2 groups was observed ($P=.955$ and $P=.630$, respectively). Percentage of liver cirrhosis ($P=.003$), hypertension history ($P=.044$), and liver cancer surgery/transplantation history ($P=.011$) were higher in SHD group than in the FD group. No difference of other baseline characteristics was discovered between FD group and SHD group (Table 1).

3.3. Comparison of pain NRS score, pain incidence, severity, and times between FD and SHD groups

Pain NRS score in FD group (2.72 ± 0.10) was increased compared with SHD group (2.28 ± 0.10) ($P=.002$, Fig. 2A), but no difference was discovered between 2 groups in the incidence of pain (96.8% vs 97.5%, $P=.959$, Fig. 2B). The severity of pain in FD group was higher than SHD group ($P=.027$, Fig. 2C), whereas there was no difference in times of pain between 2 groups (1.42 ± 0.06 vs 1.39 ± 0.05, $P=.744$, Fig. 2D).

3.4. Comparison of body temperature, fever incidence, severity, and lasting days between FD and SHD groups

Body temperature was elevated in FD group (37.85 ± 0.04°C) compared with SHD group (37.59 ± 0.05°C) ($P<.001$, Fig. 3A),

Table 1

Baseline characteristics.

Parameter	Total records (n=520)	FD group (n=284)	SHD group (n=236)	*P*
Age, y				.955
≥65 (n/%)	169 (32.5%)	92 (32.4%)	77 (32.6%)	
<65 (n/%)	351 (67.5%)	192 (67.6%)	159 (67.4%)	
Gender				.630
Male (n/%)	425 (81.7%)	230 (81.0%)	195 (82.6%)	
Female (n/%)	95 (18.3%)	54 (19.0%)	41 (17.4%)	
Diagnosis				.151
HCC (n/%)	435 (83.8%)	235 (82.7%)	200 (85.1%)	
Cholangiocarcinoma (n/%)	24 (4.6%)	15 (5.3%)	9 (3.8%)	
Mixed hepatocarcinoma (n/%)	6 (1.2%)	1 (0.4%)	5 (2.1%)	
Secondary liver cancer (n/%)	54 (19.4%)	33 (11.6%)	21 (8.9%)	
Hepatitis B				.189
Yes (n/%)	248 (47.7%)	128 (45.1%)	120 (50.8%)	
No (n/%)	272 (52.3%)	156 (54.9%)	116 (49.2%)	
Liver cirrhosis				**.003**
Yes (n/%)	187 (36.0%)	86 (30.3%)	101 (42.8%)	
No (n/%)	333 (64.0%)	198 (69.7%)	135 (57.2%)	
Hypertension history				**.044**
Yes (n/%)	91 (17.5%)	41 (14.4%)	50 (21.2%)	
No (n/%)	429 (82.5%)	243 (85.6%)	186 (78.8%)	
Diabetes history				.878
Yes (n/%)	34 (6.5%)	19 (6.7%)	15 (6.4%)	
No (n/%)	486 (93.5%)	265 (93.3%)	221 (93.6)	
Respiratory disease history				.172
Yes (n/%)	30 (5.8%)	20 (7.0%)	10 (4.2%)	
No (n/%)	490 (94.2%)	264 (93.0%)	226 (95.8%)	
Cardiovascular and cerebrovascular diseases history				.104
Yes (n/%)	34 (6.5%)	14 (4.9%)	20 (8.5%)	
No (n/%)	486 (93.5%)	270 (95.1%)	216 (91.5%)	
Other tumors history				
Yes (n/%)	78 (15.0%)	44 (15.5%)	34 (14.4%)	.730
No (n/%)	442 (85.0%)	240 (84.5%)	202 (85.6%)	
Yes-resection (n/%)	42 (53.8%)	24 (8.5%)	18 (7.7%)	.888
Yes-without resection (n/%)	36 (46.2%)	20 (7.0%)	16 (6.8%)	
Liver cancer surgery / transplantation history				**.011**
Yes (n/%)	133 (25.6%)	60 (21.1%)	73 (30.9%)	
No (n/%)	387 (74.4%)	224 (78.9%)	163 (69.1%)	

Data were presented as count (percentage). Comparison between 2 groups was performed by Chi-square test. $P<.05$ was considered significant.
DEB-TACE=drug-eluting beads transarterial chemoembolization, FD=first DEB-TACE, HCC=hepatocellular cancer, SHD=second or higher DEB-TACE.
Bold values were *P* values that were <.05.

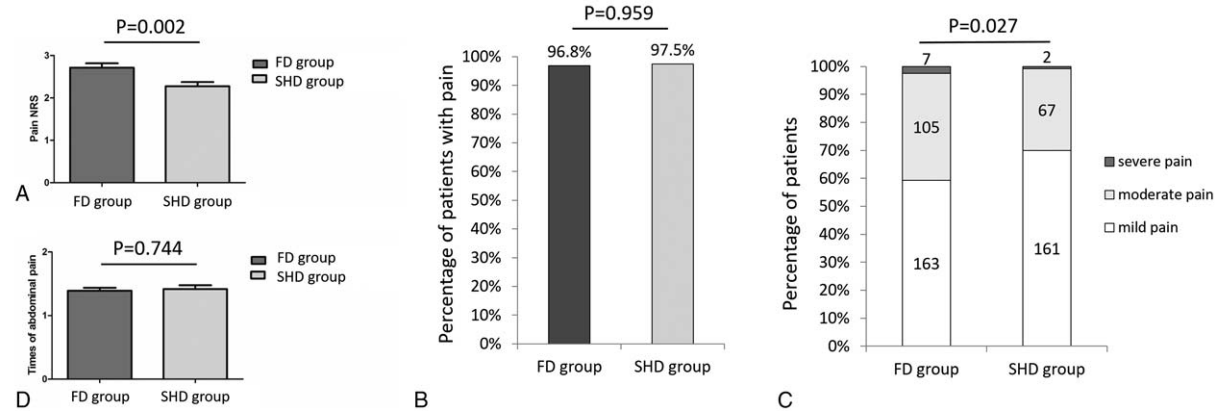

Figure 2. Comparison of Pain NRS score, pain incidence, pain severity, and times of pain between 1st DEB-TACE and 2nd or higher DEB-TACE groups. (A) Comparison of pain NRS score between 1st DEB-TACE and 2nd or higher DEB-TACE groups. (B) Comparison of pain incidence between 1st DEB-TACE and 2nd or higher DEB-TACE groups. (C) Comparison of pain severity between 1st DEB-TACE and 2nd or higher DEB-TACE groups. (D) Comparison of times of pain between 1st DEB-TACE and 2nd or higher DEB-TACE groups. Comparison between groups was performed by *t* test or Chi-square test. $P < .05$ was considered significant.

although no difference of fever incidence was disclosed between 2 groups (72.9% vs 61.4%, $P = .221$, Fig. 3B). In aspect of severity of fever, the severity grade was increased in FD group compared with SHD group ($P = .014$, Fig. 3C). Besides, the lasting days of fever in FD group (1.19 ± 0.06) were longer than SHD group (0.92 ± 0.06) ($P = .002$, Fig. 3D).

3.5. Comparison of incidence of vomiting and increased blood pressure between FD and SHD groups

As presented in Fig. 4, vomiting incidence ($P = .517$) in FD group was similar to that of SHD group, and there was no difference of increased blood pressure incidence ($P = .248$) between FD group and SHD group (Fig. 5).

3.6. Subgroups analysis of pain, fever, vomiting, and increased blood pressure in FD group

In FD group, cases with history of liver cancer surgery/transplantation correlated with lower incidence of pain ($P = .010$). Besides, cases with HCC ($P < .001$), liver cirrhosis ($P = .016$), diabetes history ($P = .021$), and liver cancer surgery/transplantation history ($P = .029$) were correlated with decreased pain severity grade (Table 2).

As summarized in Table 3, cases with diabetes history were associated with reduced rate of fever ($P = .040$); besides, age ≥65 years was associated with decreased high fever ($P = .022$).

Age ≥65 years ($P = .004$), male ($P = .002$), CCA ($P < .001$), and no other tumors history ($P < .001$) were correlated with lower possibility of vomiting in FD group (Table 4). Liver cirrhosis ($P = .011$) was associated with less occurrence of increased blood pressure, while hypertension history ($P < .001$) elevated the probability of increased blood pressure (Table 5).

3.7. Subgroups analysis of pain, fever, vomiting, and increased blood pressure in SHD Group

In SHD group, no baseline characteristics were associated with occurrence of pain (all $P > .05$), while cases with age ≥65 years ($P = .072$) and no liver cancer surgery/transplantation history

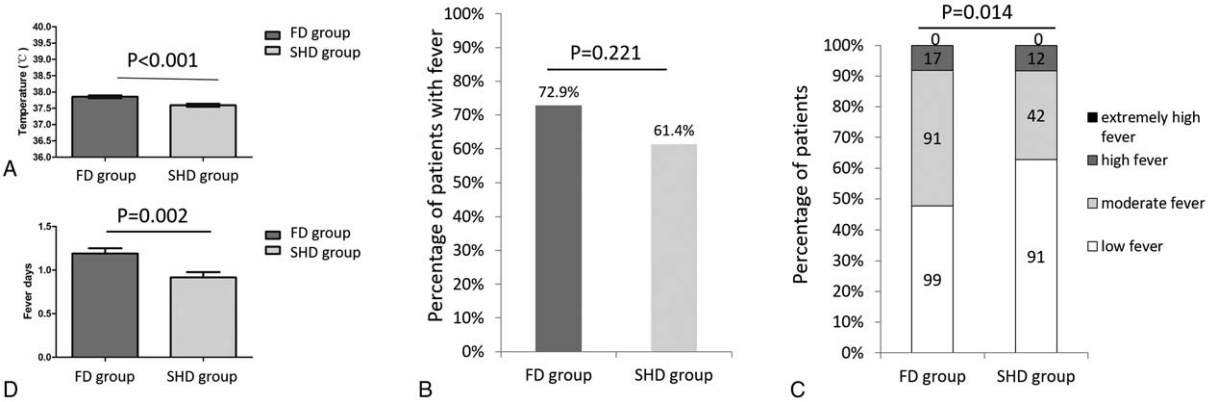

Figure 3. Comparison of temperature, fever incidence, fever severity, and days of fever between 1st DEB-TACE and 2nd or higher DEB-TACE. (A) Comparison of temperature between 1st DEB-TACE and 2nd or higher DEB-TACE groups. (B) Comparison of fever incidence between 1st DEB-TACE and 2nd or higher DEB-TACE groups. (C) Comparison of fever severity between 1st DEB-TACE and 2nd or higher DEB-TACE groups. (D) Comparison of days of fever between 1st DEB-TACE and 2nd or higher DEB-TACE groups. Comparison between groups was performed by *t* test or Chi-square test. $P < .05$ was considered significant.

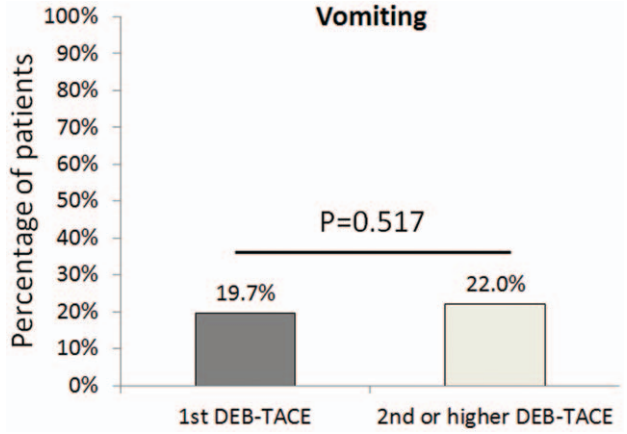

Figure 4. Comparison of incidence of vomiting between 1st DEB-TACE and 2nd or higher DEB-TACE. Comparison of vomiting incidence between 1st DEB-TACE and 2nd or higher DEB-TACE groups. Comparison between groups was performed by Chi-square test. $P < .05$ was considered significant.

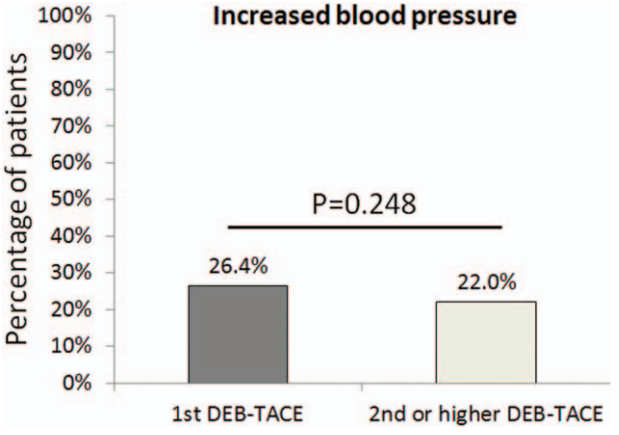

Figure 5. Comparison of incidence of increased blood pressure between 1st DEB-TACE and 2nd or higher DEB-TACE. Comparison of increased blood pressure incidence between 1st DEB-TACE and 2nd or higher DEB-TACE groups. Comparison between groups was performed by Chi-square test. $P < .05$ was considered significant.

Table 2

Subgroups analysis of pain in FD group.

Parameter	Pain (n = 275)	No pain (n = 9)	*P*	Mild pain (n = 163)	Moderate pain (n = 105)	Severe pain (n = 7)	*P*
Age, y			.951				.179
≥65 (n/%)	89 (96.7%)	3 (3.3%)		54 (60.7%)	35 (39.3%)	0 (0.0%)	
<65 (n/%)	186 (96.9%)	6 (3.1%)		109 (58.6%)	70 (37.6%)	7 (3.8%)	
Gender			.140				.759
Male (n/%)	221 (96.1%)	9 (3.9%)		130 (58.8%)	86 (38.9%)	5 (2.3%)	
Female (n/%)	54 (100.0%)	0 (0.0%)		33 (61.1%)	19 (35.2%)	2 (3.7%)	
Diagnosis			.585				**<.001**
HCC (n/%)	226 (96.2%)	9 (3.8%)		138 (61.1%)	82 (36.3%)	6 (2.7%)	
Cholangiocarcinoma (n/%)	15 (100.0%)	0 (0.0%)		6 (40.0%)	9 (60.0%)	0 (0.0%)	
Mixed hepatocarcinoma (n/%)	1 (100.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	1 (100.0%)	
Secondary liver cancer (n/%)	33 (100.0%)	0 (0.0%)		19 (57.6%)	14 (42.4%)	0 (0.0%)	
Hepatitis B			.186				.265
Yes (n/%)	122(95.3%)	6 (4.7%)		73 (59.8%)	48 (39.3%)	1 (0.8%)	
No (n/%)	119 (76.3%)	37 (23.7%)		90 (58.8%)	57 (37.3%)	6 (3.9%)	
Liver cirrhosis			.203				**.016**
Yes (n/%)	85 (98.8%)	1 (1.2%)		60 (70.6%)	25 (29.4%)	0 (0.0%)	
No (n/%)	190 (96.0%)	8 (4.0%)		103 (54.2%)	80 (42.1%)	7 (3.7%)	
Hypertension history			.773				.902
Yes (n/%)	40 (97.6%)	1 (2.4%)		25 (62.5%)	14 (35.0%)	1 (2.5%)	
No (n/%)	235 (96.7%)	8 (3.3%)		138 (58.7%)	91 (38.7%)	6 (2.6%)	
Diabetes history			.414				**.021**
Yes (n/%)	19 (100.0%)	0 (0.0%)		17 (89.5%)	2 (10.5%)	0 (0.0%)	
No (n/%)	256 (96.6%)	9 (3.4%)		146 (57.0%)	103 (40.2%)	7 (2.7%)	
Respiratory disease history			.628				.181
Yes (n/%)	19 (95.0%)	1 (5.0%)		15 (78.9%)	4 (21.1%)	0 (0.0%)	
No (n/%)	256 (97.0%)	8 (3.0%)		148 (57.8%)	101 (39.5%)	7 (2.7%)	
Cardiovascular and cerebrovascular diseases history			.488				.113
Yes (n/%)	14 (100.0%)	0 (0.0%)		11 (78.6%)	2 (14.3%)	1 (7.1%)	
No (n/%)	261 (96.7%)	9 (3.3%)		152 (58.2%)	103 (39.5%)	6 (2.3%)	
Other tumors history							
Yes (n/%)	44 (100.0%)	0 (0.0%)	.192	29 (65.9%)	14 (31.8%)	1 (2.3%)	.619
No (n/%)	231 (96.3%)	9 (3.7%)		134 (58.0%)	91 (39.4%)	6 (2.6%)	
Yes-resection (n/%)	25 (100.0%)	0 (0.0%)	1.000	16 (64.0%)	8 (32.0%)	1 (4.0%)	.398
Yes-without resection (n/%)	19 (100.0%)	0 (0.0%)		13 (68.4%)	6 (31.6%)	0 (0.0%)	
Liver cancer surgery / transplantation history			**.010**				**.029**
Yes (n/%)	55 (91.7%)	5 (8.3%)		34 (61.8%)	17 (30.9%)	4 (7.3%)	
No (n/%)	220 (98.2%)	4 (1.8%)		129 (58.6%)	88 (40.0%)	3 (1.4%)	

Data were presented as count (percentage). Comparison between 2 groups or among 3 groups was performed by Chi-square test. $P < .05$ was considered significant.
DEB-TACE = drug-eluting beads transarterial chemoembolization, FD = first DEB-TACE, HCC = hepatocellular cancer.
Bold values were *P* values that were <.05.

Table 3

Subgroups analysis of fever in FD group.

Parameter	Fever (n=207)	No fever (n=77)	*P*	Low fever (n=99)	Moderate fever (n=91)	High fever (n=17)	*P*
Age, y			.788				**.022**
≥65 (n/%)	68 (73.9%)	24 (26.1%)		28 (41.2%)	38 (55.9%)	2 (2.9%)	
<65 (n/%)	139 (72.4%)	53 (27.6%)		71 (51.1%)	53 (38.1%)	15 (10.8%)	
Gender			.577				.582
Male (n/%)	166 (72.2%)	64 (27.8%)		80 (48.2%)	74 (44.6%)	12 (7.2%)	
Female (n/%)	41 (75.9%)	13 (24.1%)		19 (46.3%)	17 (41.5%)	5 (12.2%)	
Diagnosis			.689				.879
HCC (n/%)	174 (74.0%)	61 (26.0%)		81 (46.6)	78 (44.8%)	15 (8.6%)	
Cholangiocarcinoma (n/%)	10 (66.7%)	5 (33.3%)		6 (60.0%)	3 (30.0%)	1 (10.0%)	
Mixed hepatocarcinoma (n/%)	1 (100.0%)	0 (0.0%)		1 (100.0%)	0 (0.0%)	0 (0.0%)	
Secondary liver cancer (n/%)	22 (66.7%)	11 (33.3%)		11 (50.0%)	10 (45.5%)	1 (4.5%)	
Hepatitis B			.377				.422
Yes (n/%)	90 (70.3%)	38 (29.7%)		40 (44.4%)	44 (48.9%)	6 (6.7%)	
No (n/%)	117 (75.0%)	39 (25.0%)		59 (50.4%)	47 (40.2%)	11 (9.4%)	
Liver cirrhosis			.285				.146
Yes (n/%)	59 (68.6%)	27 (31.4%)		24 (40.7%)	32 (54.2%)	3 (5.1%)	
No (n/%)	148 (74.7%)	50 (25.3%)		75(50.7%)	59 (39.9%)	14 (9.5%)	
Hypertension history			.273				.099
Yes (n/%)	27 (65.9%)	14 (34.1%)		18 (66.7%)	7 (25.9%)	2 (7.4%)	
No (n/%)	180 (74.1%)	63 (25.9%)		81 (45.0%)	84 (46.7%)	15 (8.3%)	
Diabetes history			**.040**				.204
Yes (n/%)	10 (52.6%)	9 (47.4%)		3 (30.0%)	7 (70.0%)	0 (0.0%)	
No (n/%)	197 (74.3%)	68 (25.7%)		96(48.7%)	84 (42.6%)	17(8.6%)	
Respiratory disease history			.826				.461
Yes (n/%)	15 (75.0%)	5 (25.0%)		5 (33.3%)	8 (53.3%)	2 (13.3%)	
No (n/%)	192 (72.7%)	72 (27.3%)		94 (49.0%)	83 (43.2%)	15 (7.8%)	
Cardiovascular and cerebrovascular diseases history			.268				.122
Yes (n/%)	12 (85.7%)	2 (14.3%)		8 (66.7%)	2 (16.7%)	2 (16.7%)	
No (n/%)	195 (72.2%)	75 (27.8%)		91(46.7%)	89 (45.6%)	15 (7.7%)	
Other tumors history							
Yes (n/%)	28 (63.6%)	16 (36.4%)	.133	11 (39.3%)	15 (53.6%)	2 (7.1%)	.544
No (n/%)	179 (74.6%)	61 (36.4%)		88 (49.2%)	76 (42.5%)	15 (8.4%)	
Yes-resection (n/%)	11 (55.0%)	9 (45.0%)	.236	3 (27.3%)	8 (72.7%)	0 (100.0%)	.254
Yes-without resection (n/%)	18 (72.0%)	7 (28.0%)		8 (44.4)	8 (44.4%)	2 (11.2%)	
Liver cancer surgery / transplantation history			.571				.095
Yes (n/%)	42 (70.0%)	18 (30.0%)		22 (52.4%)	20 (47.6%)	0 (0.0%)	
No (n/%)	165 (73.7%)	59 (26.3%)		77 (46.7%)	71 (43.0%)	17 (10.3%)	

Data were presented as count (percentage). Comparison between 2 groups or among 3 groups was performed by Chi-square test. $P < .05$ was considered significant.
DEB-TACE = drug-eluting beads transarterial chemoembolization, FD = first DEB-TACE, HCC = hepatocellular cancer.
Bold values were *P* values that were <.05.

(*P* = .097) seemed to have a decreased rate of pain, but no statistical significance (Table 6). As to pain severity, age ≥65 years (*P* = .042) was correlated with diminished pain severity degree, while diabetes history (*P* = .038) were associated with increased pain severity (Table 6).

Other tumor history was correlated with lower rate of fever (*P* = .001, Table 7). In addition, cases with age ≥65 years presented with lower severity of fever (*P* = .033, Table 7).

Male (*P* = .001) and liver cirrhosis (*P* = .021) decreased the possibility of vomiting (Table 8). Age ≥65 years (*P* = .043), diabetes history (*P* = .017), and other tumor history (*P* = .014) elevated the probability of increased blood pressure, while male was correlated with lower possibility of increased blood pressure (Table 9).

4. Discussion

In this study, we found that the common AEs (including pain and fever) incidence and severity were lower in SHD group than in FD group, which indicated patients receiving more cycles of DEB-TACE had higher tolerance to the operation than the first cycle; Patients with age ≥65 years presented with lower severity of pain and fever, as well as vomiting incidence; and Males were correlated with less vomiting and less increased blood pressure; diabetes history was associated with lower severity of pain, less fever, but more incidence of increased blood pressure in FD group.

DEB-TACE, made of superabsorbent polymer, has the ability of absorbing the chemotherapeutic drugs and slowly releasing them over several days (up to 14 days) in a steadily sustained manner after being administrated in liver cancer by intra-arterial injection.[14] Whereas in cTACE operation, there is a peak on the bloodstream of the chemotherapeutic agent right after the procedure and increased the occurrence of AEs.[15]

According to clinical practice guidelines proposed by the Japan Society of Hepatology, patients with intermediate stage of liver cancer could repeat TACE treatment several times or even ≥10 times before the TACE refractoriness.[16] Furthermore, to guide

Table 4

Subgroups analysis of vomiting in FD group.

Parameter	Vomiting (n=56)	No vomiting (n=228)	P
Age, y			**.004**
≥65 (n/%)	9 (9.8%)	83 (90.2%)	
<65 (n/%)	47 (24.5%)	145 (75.5%)	
Gender			**.002**
Male (n/%)	37 (16.1%)	193 (83.9%)	
Female (n/%)	19 (35.2%)	35 (64.8%)	
Diagnosis			**<.001**
HCC (n/%)	39 (16.6%)	196 (83.4%)	
Cholangiocarcinoma (n/%)	1 (6.7%)	14 (93.3%)	
Mixed hepatocarcinoma (n/%)	1 (100.0%)	0 (0.0%)	
Secondary liver cancer (n/%)	15 (45.5%)	18 (54.5%)	
Hepatitis B			.943
Yes (n/%)	25 (19.5%)	103 (80.5%)	
No (n/%)	31 (19.9%)	125 (80.1%)	
Liver cirrhosis			.525
Yes (n/%)	15 (17.4%)	71 (82.6%)	
No (n/%)	41 (20.7%)	157 (79.3%)	
Hypertension history			.698
Yes (n/%)	9 (22.0%)	32 (78.0%)	
No (n/%)	47 (19.3%)	196 (80.7%)	
Diabetes history			.297
Yes (n/%)	2 (10.5%)	17 (89.5%)	
No (n/%)	54 (20.4%)	211 (79.6%)	
Respiratory disease history			.582
Yes (n/%)	3 (15.0%)	17 (85.0%)	
No (n/%)	53 (20.1%)	211 (79.9%)	
Cardiovascular and cerebrovascular diseases history			.393
Yes (n/%)	4 (28.6%)	10 (71.4%)	
No (n/%)	52 (19.3%)	218 (80.7%)	
Other tumors history			
Yes (n/%)	17 (38.6%)	27 (61.4%)	**.001**
No (n/%)	39 (16.3%)	201 (83.7%)	
Yes-resection (n/%)	8 (42.1%)	11 (57.9%)	.680
Yes-without resection (n/%)	9 (36.0%)	16 (64.0%)	
Liver cancer surgery / transplantation history			.128
Yes (n/%)	16 (26.7%)	44 (73.3%)	
No (n/%)	40 (17.9%)	184 (82.1%)	

Data were presented as count (percentage). Comparison between 2 groups was performed by Chi-square test. $P < .05$ was considered significant.

DEB-TACE = drug-eluting beads transarterial chemoembolization, FD = first DEB-TACE, HCC = hepatocellular cancer.

Bold values were P values that were <.05.

Table 5

Subgroups analysis of increased blood pressure in FD group.

Parameter	Increased blood pressure (n=75)	No increased blood pressure (n=209)	P
Age, y			.437
≥65 (n/%)	27 (29.3%)	65 (70.7%)	
<65 (n/%)	48 (25.0%)	144 (75.0%)	
Gender			.347
Male (n/%)	58 (25.2%)	172 (74.8%)	
Female (n/%)	17 (31.5%)	37 (68.5%)	
Diagnosis			.134
HCC (n/%)	57 (24.3%)	178 (75.7%)	
Cholangiocarcinoma (n/%)	6 (40.0%)	9 (60.0%)	
Mixed hepatocarcinoma (n/%)	1 (100.0%)	0 (0.0%)	
Secondary liver cancer (n/%)	11 (33.3%)	22 (66.7%)	
Hepatitis B			.194
Yes (n/%)	29 (22.7%)	99 (77.3%)	
No (n/%)	46 (29.5%)	110 (70.5%)	
Liver cirrhosis			**.011**
Yes (n/%)	14 (16.3%)	72 (83.7%)	
No (n/%)	61 (30.8%)	137 (69.2%)	
Hypertension history			**<.001**
Yes (n/%)	21 (51.2%)	20 (48.8%)	
No (n/%)	54 (22.2%)	189 (77.8%)	
Diabetes history			.286
Yes (n/%)	7 (36.8%)	12 (63.2%)	
No (n/%)	68 (25.7%)	197 (74.3%)	
Respiratory disease history			.500
Yes (n/%)	4 (20.0%)	16 (80.0%)	
No (n/%)	71 (26.9%)	193 (73.1%)	
Cardiovascular and cerebrovascular diseases history			.152
Yes (n/%)	6 (42.9%)	8 (57.1%)	
No (n/%)	69 (25.6%)	201 (74.4%)	
Other tumors history			
Yes (n/%)	14 (31.8%)	30 (68.2%)	.376
No (n/%)	61 (25.4%)	179 (74.6%)	
Yes-resection (n/%)	9 (47.4%)	10 (52.6%)	.054
Yes-without resection (n/%)	5 (20.0%)	20 (80.0%)	
Liver cancer surgery / transplantation history			.348
Yes (n/%)	13 (21.7%)	47 (78.3%)	
No (n/%)	62 (27.7%)	162 (72.3%)	

Data were presented as count (percentage). Comparison between 2 groups was performed by Chi-square test. $P < .05$ was considered significant.

DEB-TACE = drug-eluting beads transarterial chemoembolization, FD = first DEB-TACE, HCC = hepatocellular cancer.

Bold values were P values that were <.05.

the decision for retreatment with TACE, some studies have established an objective point score assessment (ART score: Assessment for Retreatment with TACE).[17,18] A previous study including patients treated by retreatment of cTACE or DEB-TACE illuminates that HCC patients with ART score ≥2.5 points before the second cycle of treatment have worse prognosis, which has been validated in a larger sample.[17,19] Those results also indicate that there are HCC patients who benefit from cTACE or DEB-TACE retreatments. In our study, the results showed that AE incidence of pain and fever in SHD group was lower than FD group; the possible reasons might be as follows: pain and fever are primarily caused by necrosis of tumor tissue that promotes inflammatory responses in patients, which might be a possible explanation of the reduced incidence and severity of pain and fever in SHD group due to that there was less necrosis of tumor tissue after second or multiple treatments[20,21]; and threshold value of pain and fever increases after first cycle of DEB-TACE operation; thus, more tolerance is presented in subsequent cycles of DEB-TACE operation. However, no difference of vomiting and increased blood pressure was discovered between FD and SHD groups. The possible explanations might be vomiting and increased blood pressure are much less frequent compared with pain and fever in DEB-TACE; thus, the influence of treatment cycles on vomiting and increased blood pressure is less; vomiting is mainly caused by chemotherapeutics, the dose and type of which were similar in 2 groups; therefore, no difference in vomiting incidence was found between FD and SHD groups; and increased blood pressure is a consequence of the side effect of chemotherapeutics and the embolic effect in artery caused by embolization procedure in DEB-TACE operation. Therefore, a possible explanation to the similar incidence of increased blood pressure in 2 groups might be that the chemotherapeutics and

Table 6

Subgroups analysis of pain in SHD group.

Parameter	Pain (n = 230)	No pain (n = 6)	*P*	Mild pain (n = 161)	Moderate pain (n = 67)	Severe pain (n = 2)	*P*
Age, y			.072				**.042**
≥65 (n/%)	73 (94.8%)	4 (5.2%)		59 (80.8%)	14 (19.2%)	0 (0.0%)	
<65 (n/%)	157 (98.7%)	2 (1.3%)		102 (65.0%)	53 (33.8%)	2 (1.3%)	
Gender			.963				.463
Male (n/%)	190 (97.4%)	5 (2.6%)		130 (68.4%)	58 (30.5%)	2 (1.1%)	
Female (n/%)	40 (97.6%)	1 (2.4%)		31 (77.5%)	9 (22.5%)	0 (0.0%)	
Diagnosis			.072				.970
HCC (n/%)	196 (98.0%)	4 (2.0%)		139 (70.9%)	55 (28.1%)	2 (1.0%)	
Cholangiocarcinoma (n/%)	9 (100.0%)	0 (0.0%)		6 (66.7%)	3 (33.3%)	0 (0.0%)	
Mixed hepatocarcinoma (n/%)	4 (80%)	1 (20.0%)		2 (50.0%)	2 (50.0%)	0 (0.0%)	
Secondary liver cancer (n/%)	20 (95.2%)	1 (4.8%)		14 (70.0%)	6 (30.0%)	0 (0.0%)	
Hepatitis B			.966				.951
Yes (n/%)	117 (97.5%)	3 (2.5%)		78 (69.0%)	34 (30.1%)	1 (0.9%)	
No (n/%)	113 (97.4%)	3 (2.6%)		83 (70.9%)	33 (28.2%)	1 (0.9%)	
Liver cirrhosis			.718				.264
Yes (n/%)	98 (97.0%)	3 (3.0%)		74 (75.5%)	23 (23.5%)	1 (1.0%)	
No (n/%)	132 (97.8%)	3 (2.2%)		87 (65.9%)	44 (33.3%)	1 (0.8%)	
Hypertension history			.198				.324
Yes (n/%)	50 (100.0%)	0 (0.0%)		39 (78.0%)	11 (22.0%)	0 (0.0%)	
No (n/%)	180 (96.8%)	6 (3.2%)		122 (67.8%)	56 31.1%)	2 (1.1%)	
Diabetes history			.518				**.038**
Yes (n/%)	15 (100.0%)	0 (0.0%)		9 (60.0%)	5 (33.3%)	1 (6.7%)	
No (n/%)	215 (97.3%)	6 (2.7%)		152 (70.7%)	62 (28.8%)	1 (0.5%)	
Respiratory disease history			.602				.717
Yes (n/%)	10 (100.0%)	0 (0.0%)		6 (60.0%)	4 (40.0%)	0 (0.0%)	
No (n/%)	220 (97.3%)	6 (2.7%)		155 (70.5%)	63 (28.6%)	2(0.9%)	
Cardiovascular and cerebrovascular diseases history			.450				.820
Yes (n/%)	20 (100.0%)	0 (0.0%)		15 (75.0%)	5 (25.0%)	0 (0.0%)	
No (n/%)	210 (97.2%)	6 (2.8%)		146 (69.5%)	62 (29.5%)	2(1.0%)	
Other tumors history							
Yes (n/%)	33 (97.1%)	1 (2.9%)	.873	26 (78.8%)	7 (21.2%)	0 (0.0%)	.452
No (n/%)	197 (97.5%)	5 (2.5%)		135 (68.5%)	60 (30.5%)	2(1.0%)	
Yes-resection (n/%)	15 (93.8%)	1 (6.2%)	.282	10 (66.7%)	5 (33.3%)	0 (0.0%)	.120
Yes-without resection (n/%)	18 (100.0%)	0 (0.0%)		16 (88.9%)	2 (11.1%)	0(0.0%)	
Liver cancer surgery / transplantation history			.097				.238
Yes (n/%)	73 (100.0%)	0 (0.0%)		56 (76.7%)	17 (23.3%)	0 (0.0%)	
No (n/%)	157 (96.3%)	6 (3.7%)		105 (66.9%)	50 (31.8%)	2(1.3%)	

Data were presented as count (percentage). Comparison between 2 groups or among 3 groups was performed by Chi-square test. $P < .05$ was considered significant.
DEB-TACE = drug-eluting beads transarterial chemoembolization, HCC = hepatocellular cancer, SHD = second or higher DEB-TACE.
Bold values were *P* values that were <.05.

embolic agents, namely the microbeads, were of no difference between 2 groups.[22,23]

Due to the diversified physical conditions, clinical properties, and biological features, the incidence of AEs in patients receiving DEB-TACE treatment differs from each other.[8,24] However, the most common AEs are abdominal pain, fever, nausea and vomiting, increase blood pressure, and severe side effects such as hepatic decompensation, gastrointestinal bleeding, or treatment-related death of the patients treated with DEB-TACE.[25,26] Thus, in order to better optimize the efficacy of DEB-TACE treatment, it is essential to explore factors which are associated with the incidence of common AEs both in first DEB-TACE treated patients and repeatedly DEB-TACE treated patients. In our study, we observed that patients with age ≥65 years presented with lower severity of pain and fever, as well as vomiting incidence, which might result from elderly patients aged ≥65 years presented with lower metabolism and less sensitivity to pain; thus, the severity of pain was decreased; The decreased severity of pain reduced the use of analgesic drug; thus, vomiting was decreased accordingly; and elderly people aged ≥65 years were with decreased immunity, hence most of them suffer from low and moderate degrees of fever.[27] Besides, we also found diabetes history and male are associated with lower severity of pain and probability of vomiting, respectively. Although the exact reasons why these factors were correlated with less severity of AEs was unclear, the explanations might be diabetes cause peripheral neuropathy and central neuropathy to decline the sense of pain[28–30]; female increased the possibility of vomiting, which was in line with the study conducted by Schiller et al[31] that nausea and vomiting are more frequent when patients are female experiencing intensity-modulated radiation therapy, but the reason is unclear.

This was the first study analyzing the differences of common AEs between FD and SHD treatments, and further exploring the comprehensive factors affecting common AEs in both FD and SHD groups. However, there were some limitations in this study. First, the operations of DEB-TACE were performed by a group of

Table 7

Subgroups analysis of fever in SHD group.

Parameter	Fever (n=145)	No fever (91)	P	Low fever (n=91)	Moderate fever (n=42)	High fever (n=12)	P
Age, y			.130				**.033**
≥65 (n/%)	42 (54.5%)	35 (45.5%)		33 (78.6%)	8 (19.0%)	1 (2.4%)	
<65 (n/%)	103 (64.8%)	56 (35.2%)		58 (56.3%)	34 (33.0%)	11 (10.7%)	
Gender			.179				.396
Male (n/%)	116 (59.5%)	79 (40.5%)		70 (60.3%)	35 (30.2%)	11(9.5%)	
Female (n/%)	29 (70.7%)	12 (29.3%)		21 (72.4%)	7 (24.1%)	1 (3.4%)	
Diagnosis			.116				.582
HCC (n/%)	129 (64.5%)	71 (35.5%)		78 (60.5%)	39 (30.2%)	12 (9.3%)	
Cholangiocarcinoma (n/%)	4 (44.4%)	5 (55.6%)		4 (100.0%)	0 (0.0%)	0 (0.0%)	
Mixed hepatocarcinoma (n/%)	2 (40.0%)	3 (60.0%)		2 (100.0%)	0 (0.0%)	0 (0.0%)	
Secondary liver cancer (n/%)	9 (42.9%)	12 (57.1%)		6 (66.7%)	3 (33.3%)	0 (0.0%)	
Hepatitis B			.253				.224
Yes (n/%)	78 (65.0%)	42 (35.0%)		47 (70.1%)	16 (23.9%)	4(6.0%)	
No (n/%)	67 (57.8%)	49 (42.2%)		44 (56.4%)	26 (33.3%)	8 (10.3%)	
Liver cirrhosis			.426				.283
Yes (n/%)	65 (64.4%)	36 (35.6%)		39 (60.0%)	18 (27.7%)	8 (12.4%)	
No (n/%)	80 (59.3%)	55 (40.7%)		52 (65.0%)	24 (30.0%)	4 (5.0%)	
Hypertension history			.675				.145
Yes (n/%)	32 (64.0%)	18 (36.0%)		21 (65.6%)	11 (34.4%)	0 (0.0%)	
No (n/%)	113 (60.8%)	73 (39.2%)		70 (61.9%)	31 (27.4%)	12 (10.6%)	
Diabetes history			.224				0.412
Yes (n/%)	7 (46.7%)	8 (53.3%)		6 (85.7%)	1 (14.3%)	0 (0.0%)	
No (n/%)	138 (62.4%)	83 (37.6%)		85 (61.6%)	41 (29.7%)	12 (8.7%)	
Respiratory disease history			.058				.889
Yes (n/%)	9 (90.0%)	1 (10.0%)		5 (55.6%)	3 (33.3%)	1 (11.1%)	
No (n/%)	136 (60.2%)	90 (39.8%)		86 (63.2%)	39 (28.7%)	11 (8.1%)	
Cardiovascular and cerebrovascular diseases history			.536				.328
Yes (n/%)	11 (55.0%)	9 (45.0%)		6 (54.5%)	5 (45.5%)	0 (0.0%)	
No (n/%)	134 (62.0%)	82 (38.0%)		85 (63.4%)	37 (27.6%)	12 (9.0%)	
Other tumors history							
Yes (n/%)	12 (35.3%)	22 (64.7%)	**.001**	7 (58.3%)	5 (41.7%)	0 (0.0%)	.396
No (n/%)	133 (65.8%)	69 (34.2%)		84 (63.2%)	37 (27.8%)	12 (9.0%)	
Yes-resection (n/%)	3 (18.8%)	13 (81.3%)	.057	2 (66.7%0	1 (33.3%)	0 (0.0%)	.735
Yes-without resection (n/%)	9 (50.0%)	9 (50.0%)		5 (55.65)	4 (44.4%)	0 (0.0%)	
Liver cancer surgery / transplantation history			.409				.671
Yes (n/%)	42 (57.5%)	31 (42.5%)		28 (66.7%)	10 (23.8%)	4 (9.5%)	
No (n/%)	103 (63.2%)	60 (36.8%)		63 (61.2%)	32 (31.1%)	8 (7.8%)	

Data were presented as count (percentage). Comparison between 2 groups or among 3 groups was performed by Chi-square test. $P < .05$ was considered significant.
DEB-TACE = drug-eluting beads transarterial chemoembolization, HCC = hepatocellular cancer, SHD = second or higher DEB-TACE.
Bold values were P values that were <.05.

doctors, which could cause confounding factors by diverse degrees of skill of physicians, but our study with the large sample would reduce the influence of confounding factors. Second, this was a single-centered, retrospective cohort study; thus, a prospective, interventional study is greatly needed. Third, cases with mixed hepatocarcinoma were relatively small (N = 5) leading to less statistical power and the safety profile of DEB-TACE in mixed hepatocarcinoma patients was not fully analyzed, hence a comprehensive analysis including a greater number of mixed hepatocarcinoma cases of common AEs is needed in the future. Finally, there might be selection bias due to that it is likely patients will not receive second DEB-TACE treatment if severe AE exists after their first treatment, which might lead to a larger proportion of patients in SHD group were patients with satisfying AE profiles. However, this bias of our study might be very limited because that the severe AEs of DEB-TACE treatment are very rare, and in clinical practice, the predominant reason of patients receiving multiple cycles of DEB-TACE treatment is lacking efficacy but not a satisfying AE profile of first treatment.[8,32,33] The AE profile post first DEB-TACE should be compared with that of multiple DEB-TACE treatments by future studies.

In conclusion, SHD was better tolerated than FD in liver cancer patients, and older age as well as male were correlated with less occurrence or severity of common AEs in DEB-TACE operation.

Author contributions

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Table 8

Comprehensive analysis of vomiting in 2nd or higher DEB-TACE.

Parameter	Vomiting (n = 52)	No vomiting (n = 184)	*P*
Age, y			.991
≥65 (n/%)	17 (22.1%)	60 (77.9%)	
<65 (n/%)	35 (22.0%)	124 (78.0%)	
Gender			**.001**
Male (n/%)	35 (17.9%)	160 (82.1%)	
Female (n/%)	17 (41.5%)	24 (58.5%)	
Diagnosis			.474
HCC (n/%)	41 (20.5%)	159 (79.5%)	
Cholangiocarcinoma (n/%)	3 (33.3%)	6 (66.7%)	
Mixed hepatocarcinoma (n/%)	1 (20.0%)	4 (80.0%)	
Secondary liver cancer (n/%)	7 (33.3%)	14 (66.7%)	
Hepatitis B			.280
Yes (n/%)	23 (19.2%)	97 (80.8%)	
No (n/%)	29 (25.0%)	87 (75.0%)	
Liver cirrhosis			**.021**
Yes (n/%)	15 (14.9%)	86 (85.1%)	
No (n/%)	37 (27.4%)	98 (72.6%)	
Hypertension history			.438
Yes (n/%)	9 (18.0%)	41 (82.0%)	
No (n/%)	43 (23.1%)	143 (76.9%)	
Diabetes history			.138
Yes (n/%)	1 (6.7%)	14 (93.3%)	
No (n/%)	51 (23.1%)	170 (76.9%)	
Respiratory disease history			.874
Yes (n/%)	2 (20.0%)	8 (80.0%)	
No (n/%)	50 (22.1%)	176 (77.9%)	
Cardiovascular and cerebrovascular diseases history			.175
Yes (n/%)	2 (10.0%)	18 (90.0%)	
No (n/%)	50 (23.1%)	166 (76.9%)	
Other tumors history			
Yes (n/%)	10 (29.4%)	24 (70.6%)	.262
No (n/%)	42 (20.8%)	160 (79.2%)	
Yes-resection (n/%)	3 (18.7%)	13 (81.3%)	.198
Yes-without resection (n/%)	7 (38.9%)	11 (61.1%)	
Liver cancer surgery / transplantation history			.183
Yes (n/%)	20 (27.4%)	53 (72.6%)	
No (n/%)	32 (19.6%)	131 (80.4%)	

Data were presented as count (percentage). Comparison between 2 groups was performed by Chi-square test. $P < .05$ was considered significant.

DEB-TACE = drug-eluting beads transarterial chemoembolization, HCC = hepatocellular cancer.

Bold values were *P* values that were <.05.

Table 9

Comprehensive analysis of blood pressure in 2nd or higher DEB-TACE.

Parameter	Increased blood pressure (n = 52)	No increased blood pressure (n = 184)	*P*
Age, y			**.043**
≥65 (n/%)	23 (29.9%)	54 (70.1%)	
<65 (n/%)	29 (18.2%)	130 (81.8%)	
Gender			**.040**
Male (n/%)	38 (19.5%)	157 (80.5%)	
Female (n/%)	14 (34.1%)	27 (65.9%)	
Diagnosis			.059
HCC (n/%)	42 (21.0%)	158 (79.0%)	
Cholangiocarcinoma (n/%)	1 (11.1%)	8 (88.9%)	
Mixed hepatocarcinoma (n/%)	0 (0.0%)	5 (100.0%)	
Secondary liver cancer (n/%)	9 (42.9%)	12 (57.1%)	
Hepatitis B			.280
Yes (n/%)	23 (19.2%)	97 (80.8%)	
No (n/%)	29 (25.0%)	87 (75.0%)	
Liver cirrhosis			.474
Yes (n/%)	20 (19.8%)	81 (80.2%)	
No (n/%)	32 (23.7%)	103 (76.3%)	
Hypertension history			.995
Yes (n/%)	11 (22.0%)	39 (78.0%)	
No (n/%)	41 (22.0%)	145 (78.0%)	
Diabetes history			**.017**
Yes (n/%)	7 (46.7%)	8 (53.3%)	
No (n/%)	45 (20.4%)	176 (79.6%)	
Respiratory disease history			.874
Yes (n/%)	2 (20.0%)	8 (80.0%)	
No (n/%)	50 (22.1%)	176 (77.9%)	
Cardiovascular and cerebrovascular diseases history			.369
Yes (n/%)	6 (30.0%)	14 (70.0%)	
No (n/%)	46 (21.3%)	170 (78.7%)	
Other tumors history			
Yes (n/%)	13 (38.2%)	21 (61.8%)	**.014**
No (n/%)	39 (19.3%)	163 (80.7%)	
Yes-resection (n/%)	7 (43.8%)	9 (56.2%)	.533
Yes-without resection (n/%)	6 (33.3%)	12 (66.7%)	
Liver cancer surgery/ transplantation history			.756
Yes (n/%)	17 (23.3%)	56 (76.7%)	
No (n/%)	35 (21.5%)	128 (78.5%)	

Data were presented as count (percentage). Comparison between 2 groups was performed by Chi-square test. $P < .05$ was considered significant.

DEB-TACE = drug-eluting beads transarterial chemoembolization, HCC = hepatocellular cancer.

Bold values were *P* values that were <.05.

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