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Initial Experience with Balloon-Occluded Trans-catheter Arterial Chemoembolization (B-TACE) for Hepatocellular Carcinoma

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Abstract
Purpose This study was performed to evaluate the accumulation of lipiodol emulsion (LE) and adverse events during our initial experience of balloon-occluded trans-catheter arterial chemoembolization (B-TACE) for hepatocellular carcinoma (HCC) compared with conventional TACE (C-TACE).
Methods B-TACE group (50 cases) was compared with C-TACE group (50 cases). The ratio of the LE concentration in the tumor to that in the surrounding embolized liver parenchyma (LE ratio) was calculated after each treatment. Adverse events were evaluated according to the Common Terminology Criteria for Adverse Effects (CTCAE) version 4.0.
Results The LE ratio at the level of subsegmental showed a statistically significant difference between the groups (t test: $P < 0.05$). Only elevation of alanine aminotransferase was more frequent in the B-TACE group, showing a statistically significant difference (Mann–Whitney test: $P < 0.05$). While B-TACE caused severe adverse events (liver abscess and infarction) in patients with bile duct dilatation, there was no statistically significant difference in incidence between the groups. Multivariate logistic regression analysis suggested that the significant risk factor for liver abscess/infarction was bile duct dilatation ($P < 0.05$).
Conclusion The LE ratio at the level of subsegmental showed a statistically significant difference between the groups (t test: $P < 0.05$). B-TACE caused severe adverse events (liver abscess and infarction) in patients with bile duct dilatation.

Keywords Hepatocellular carcinoma (HCC) · Balloon-occluded trans-catheter arterial chemoembolization (B-TACE) · Adverse events

Introduction

Trans-catheter arterial chemoembolization (TACE) is recommended as first-line palliative therapy for unresectable intermediate-stage hepatocellular carcinoma (HCC) because it improves survival compared with best supportive care [1, 2]. With advances in diagnostic imaging and treatment in recent years, implementation of radical treatment such as surgical resection and radiofrequency ablation has been increasing. However, even if curative treatment is selected as the initial treatment, the high recurrence rate of HCC due to multi-centric carcinogenesis and intrahepatic metastasis makes it difficult to achieve a cure. TACE is widely performed for multifocal HCC when curative treatment is difficult [3–10].

Irie et al. [11] reported that balloon-occluded TACE (B-TACE) is able to achieve denser accumulation of lipiodol

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emulsion (LE) in HCC than conventional TACE (C-TACE). They published a preliminary report on this phenomenon [11] and described the mechanism underlying denser accumulation of LE with B-TACE based on measurement of the balloon-occluded arterial stump pressure (BOASP) in the embolized region. B-TACE also allows forceful retrograde injection of embolic material into the collateral vessels, which may improve local control of tumor nodules.

Therefore, B-TACE has attracted considerable attention in recent years [11–13]. Irie et al. investigated the safety of B-TACE for HCC by analyzing adverse events in 82 patients [13]. They found that only elevation of alanine aminotransferase (ALT) was significantly more frequent in the B-TACE group compared with the C-TACE group. However, their study involved relatively small number of subjects and was performed in only one institution; therefore, investigation of large number of patients in more number of institutions was needed to evaluate the safety and adverse events of B-TACE.

Accordingly, this study was performed to evaluate the accumulation of LE and adverse events during our initial experience of B-TACE for HCC compared with C-TACE.

Materials and Methods

Patients

This single-center study was approved by our Institutional Review Board.

TACE is indicated for patients with intermediate-stage HCC (four or more tumors) according to the Barcelona Clinic Liver Cancer staging system. Also, in the 2010 Japan Society of Hepatology consensus-based treatment algorithm for HCC, TACE is recommended for patients in Child-Pugh class A or B with a tumor >3 cm in diameter or with ≥4 tumors [14, 15].

Eligibility criteria were Eastern Cooperative Oncology Group performance status ≤2, albumin >2.5 g/dL, ALT and aspartate aminotransferase <5 times the upper limit of normal, total bilirubin <3.0 mg/dL, and platelet count ≥30,000/mm^3. Patients with potentially resectable HCC in whom surgery was high risk because of poor liver function or poor performance status were also included in this study. Patients were also included if radiofrequency ablation was considered to be high risk because of proximity of the tumor to the hepatic hilum, liver capsule, gallbladder, gastrointestinal tract, diaphragm, or pericardium, even if they were eligible for radiofrequency therapy because of the small number and size of their tumors. Exclusion criteria were tumor thrombus in the main portal venous trunk, extrahepatic metastasis, and high-flow arterioportal or arteriovenous shunts.

Table 1 shows the characteristics of the B-TACE group and the C-TACE group. During the 6-month period from February to July 2013, only C-TACE was performed. During the 7-month period from August 2013 to February 2014, patients were assigned to either B-TACE or C-TACE.

B-TACE Procedure

All B-TACE procedures were performed by experienced interventional radiologists Mitsunari Maruyama and Tomonori Nakamura. Hepatic angiography was done via the femoral artery under local anesthesia using a 4-Fr. sheath (Super Sheath; Medikit, Tokyo, Japan), a 4-Fr. preshaped catheter (Selecon-PA Catheter; Terumo, Tokyo, Japan), and a 2.8-Fr. microcatheter (μ7; Terumo, Tokyo, Japan) to evaluate the anatomy of the hepatic artery, the tumor blood supply, and arteriovenous shunting. Computed

Table 1 Patient Characteristics

	B-TACE ($n = 50$)	C-TACE ($n = 50$)
Child-Pugh (A:B:C)	43:7:0	39:11:0
Virus (B:C:nonB-nonC)	8:30:12	7:36:7
Diameter of main target tumor (cm)	3.2 ± 2.8	2.8 ± 1.7
Mean ± SD (range)	(1.0–12)	(1.0–9.5)
1st TACE:2nd TACE*	12:38	21:29
Past history of RFA	15	17
Past history of surgical operation	19	15
Type 2 DM	16	15
Extension of bile duct**	7	3

*Only 1st TACE/2nd TACE showed a statistically significant difference between the groups (Fisher's exact test: $P < 0.05$). 2nd TACE means as a treatment for recurred lesion after TACE. **Extension of bile duct means that common bile duct diameter is more than 11 mm

RFA radiofrequency ablation, *DM* diabetes mellitus

tomography (CT) was performed during hepatic arteriography (CTHA) and during arterial portography (CTAP) using a unified angio-CT system to estimate the extent of the tumor, tumor hemodynamics, and portal blood flow. The clinical diagnosis of HCC was confirmed from the imaging findings. Imaging studies included triphasic contrast-enhanced CT (CECT) with bolus injection of contrast medium, and a combination of CTAP and CTHA at the time of B-TACE. HCC was diagnosed if a lesion showed hypervascularity in the arterial phase on both CECT and CTHA, along with a relatively low density in the portal venous phase of CECT as well as perfusion defects on CTAP. After identification of feeding arteries, B-TACE was performed using a 2.8-Fr. microballoon catheter (Attendant; Terumo, Tokyo, Japan) and a 4-Fr. preshaped catheter. For selective B-TACE, the microballoon catheter was advanced as close as possible to the target vessel.

LE was prepared by dissolving 10 mg of epirubicin (epirubicin hydrochloride for injection 10 mg 'SAWAI'; Sawai Pharmaceutical Co. Ltd., Osaka, Japan) in 1 mL of nonionic contrast medium (Omnipaque 300; Daiichi Sankyo Co. Ltd., Tokyo, Japan) and then mixing in 1–2 mL of iodinated poppy seed oil ethyl ester (Lipiodol 480; Guerbet, Tokyo, Japan). The maximum dose of epirubicin for a single B-TACE session was limited to 60 mg/m^2 of body surface area. The balloon was generally inflated to the same diameter as that of the target vessel. When we used a 2.8-Fr. microballoon catheter (φ4.5 mm × 10 mm, Attendant; Terumo, Tokyo, Japan), we filled the balloon inflation, enclosed a 1-ml syringe with mixture (the contrast medium and the heparin-added physiological saline = 1:1), connected the 1-ml syringe to the balloon lumen, and injected up to 0.2 ml by the operator hand. Blood flow in the peripheral artery was detected during balloon occlusion. LE was injected avoiding retrograde flow beyond the balloon. Injection was stopped when LE flowed into the peripheral portal vein branches of the normal liver parenchyma or when dense accumulation of LE in the tumor was confirmed. Then embolization was done with gelatin sponge particles (Gelpart: Nippon Kayaku/Astellas, Tokyo, Japan) having a diameter of 1 mm. The end-point was reached when embolization of the distal vessel occurred, and there was complete disappearance or marked reduction of the tumor stain on hepatic arteriography. We performed mild TAE in the cases with common bile duct dilatation on CT image. Common bile duct dilatation means that common bile duct diameter is more than 11 mm. We did not performe TAE in the cases with intrahepatic bile duct dilatation on CT image. Intrahepatic bile duct dilatation means that intrahepatic bile duct diameter is more than 2 mm. If the patient had multiple tumors or a large tumor occupying several segments of the liver, LE was first injected into the right or left hepatic artery (or both for bi-lobar tumors) followed by embolization with gelatin sponge particles.

C-TACE Procedure

All C-TACE procedures were performed by experienced interventional radiologists (Mitsunari Maruyama, Tomonori Nakamura). The method was similar to that of B-TACE, except that a balloon was not used. During the first 6 months of the study (February to July 2013), only C-TACE was performed. During the subsequent 7 months (August 2013 to February 2014), C-TACE was performed if the tumor stain was attenuated on digital subtraction angiography (DSA) after inflation of the balloon.

Indications for B-TACE and C-TACE

From August 2013 to February 2014, either B-TACE or C-TACE was chosen for the patients. After identification of the tumor feeding artery by hepatic angiography, a microballoon catheter was advanced as close as possible to the feeding vessel. DSA was performed before and after inflation of the balloon. If the tumor stain was similar before and after balloon inflation, B-TACE was performed. If the tumor stain was weaker after balloon inflation by thick anastomotic vessels with collateral flow, C-TACE was performed.

Assessment

Ratio of the LE Concentration in Tumor to that in Embolized Liver Parenchyma (LE Ratio)

The ratio of the LE concentration in the tumor to that in the surrounding embolized liver parenchyma (LE ratio) was calculated after each treatment. The CT values of the HCC nodules and the liver parenchyma in the embolized region were measured on the CT scan obtained immediately after TACE. If there were multiple tumors, the largest nodule was measured. To measure the tumor CT value, the axial image that showed the largest cross section of the tumor was selected, and the entire nodule was identified as the region of interest. To measure the CT value of embolized liver parenchyma, regions of interest were placed at three sites or more while avoiding vascular structures, and the average CT value was calculated.

Then, the tumor CT value was divided by the CT value of embolized liver parenchyma to calculate the LE ratio and the ratios were compared between the B-TACE group and the C-TACE group. Each TACE group was divided into three subgroups at the level of lobar, segmental, subsegmental and compares LE ratios between the subgroups.

Local Control Rate

A triphasic CECT scan for all patients was performed at 1 month after TACE. Imagings were repeated at each follow-up every 1–3 months. Local recurrence was defined as either of the following: (1) an area without lipiodol retention within the tumor after treatment, with enhancement in the contrast arterial phase, and hypodensity in the portal venous phase or (2) an area adjacent to lipiodol retention with enhancement in the contrast arterial phase and hypodensity in the portal venous phase. The local control rate was the proportion of target nodules which did not recur for all nodules during the observation period. Local control rate of target nodules in both the B-TACE group and the C-TACE group was estimated using the Kaplan–Meier method. If there were multiple tumors, we regard the largest nodule as the target nodule. The number of target nodules in the B-TACE group was 50, and that of the C-TACE group was 50. Any lesion separated from lipiodol retention, even if only slightly, was not regarded as local recurrence. Observation period was defined as the time between TACE and last evaluation.

Adverse Events

Patients underwent physical examination, clinical laboratory tests, and assessment of adverse events. Post-embolization syndrome (fever, abdominal pain, and nausea) was evaluated according to the Common Terminology Criteria for Adverse Effects (CTCAE) version 4.0 based on the requirement for medication after TACE. As an indicator of hepatocellular damage and the impact on liver function, elevation of alanine transaminase (ALT) and bilirubin was examined. Laboratory tests were conducted for 1 month after B-TACE and C-TACE.

Statistical Analysis

We compared patient characteristics, adverse events, the doses of epirubicin and Lipiodol, and the LE ratio between the B-TACE group and the C-TACE groups using Fisher's exact test, the unpaired t test, and Mann–Whitney test. Local control rate was estimated using the Kaplan–Meier method, and statistically significant differences between the groups were compared using the log-rank test. Multivariate logistic regression analysis was performed to identify factors having influence on adverse events.

A P value of less than 0.05 was considered to indicate statistical significance. All analyses were performed with SPSS software (version 17.0.0 for Windows; SPSS, Chicago, IL).

Results

From August 2013 to February 2014, B-TACE was performed in 50 patients. C-TACE was also performed in 50 patients, including 39 patients during the 6 months from February to July 2013 and 11 patients during the 7 months from August 2013 to February 2014. Both B-TACE and C-TACE were accomplished successfully with no procedural complications.

Table 1 shows the patient characteristics. Only the 1st TACE/2nd TACE ratio showed a statistically significant difference between the B-TACE group and the C-TACE group (Fisher's exact test: $P < 0.05$).

Table 2 shows the doses of epirubicin and lipiodol, as well as the LE ratios, for the B-TACE group and the C-TACE group. There were no statistically significant differences in the doses of epirubicin and lipiodol between the groups. The mean LE ratio of the B-TACE at the level of subsegmental was 8.24 (6.88–8.34), and that of the C-TACE was 4.18 (3.57–4.80). Only mean LE ratio at the level of subsegmental showed a statistically significant difference between the groups (t test: $P < 0.05$). LE ratio at the level of both lobar and segmental was higher than C-TACE, but with no statistically significant difference being noted (t test).

Figure 1 shows the local control rate of target nodules in both the B-TACE group and the C-TACE group estimated using the Kaplan–Meier method. The number of target nodules in the B-TACE group was 50, and that of the C-TACE group was 50. There was no statistically significant difference between the groups (the log-rank test).

Table 3 shows the adverse events in both the groups. Only elevation of ALT was more frequent in the B-TACE group, showing a statistically significant difference (Mann–Whitney test: $P < 0.05$). In addition, 3 patients (6 %) developed liver abscess and one patient (2 %) had liver infarction in the B-TACE, while no severe adverse events occurred in the C-TACE group. While the frequency of liver abscess/infarction was higher in the B-TACE group, there was no statistically significant difference between the groups (Fisher's exact test). The patients with these severe adverse events recovered after drainage and antibiotic therapy.

The multivariate logistic regression analysis was only done for patients in the B-TACE group. Factors associated with severe adverse events in these 4 patients subjected to multivariate logistic regression analysis were the age, tumor size, TACE at the level of lobar, the dose of epirubicin, 2nd TACE, HbA1c (NGSP), and bile duct dilatation. The results of multivariate logistic regression analysis are displayed in Table 4. Three of the 4 patients who

Table 2 The amount dose of epirubicin and lipiodol, and LE ratio at the level of lobar, segmental, and subsegmental

	B-TACE	C-TACE
Epirubicin (mg)		
Mean ± SD (range)	36.3 ± 17.0 (7.0–80.0)	34.7 ± 16.7 (10.0–90.0)
	[$n = 50$]	[$n = 50$])
Lipiodol (ml)		
Mean ± SD (range)	4.60 ± 2.58 (1.0–12.0)	3.70 ± 1.77 (1.0–8.0)
	[$n = 50$]	[$n = 50$]
LE ratio		
Mean ± SD (range)	4.48 ± 2.08 (1.8–9.91)	3.42 ± 1.57 (1.32–7.35)
	[$n = 50$]	[$n = 50$]
Lobar level	3.82 ± 1.59 (1.81–8.31)	3.12 ± 1.0 (1.32–4.81)
	[$n = 31$]	[$n = 36$]
Segmental level	4.65 ± 2.66 (2.34–9.91)	3.96 ± 1.49 (2.27–7.35)
	[$n = 16$]	[$n = 10$]
Subsegmental level*	8.24 ± 2.75 (6.88–8.34)	4.18 ± 0.44 (3.57–4.80)
	[$n = 3$]	[$n = 4$]

There was no statistically significant difference in the amount dose of epirubicin and lipiodol, LE ratio at the level of lobar and subsegmental between the groups (t test). *Only mean LE ratio at the level of subsegmental showed a statistically significant difference between the groups (t test: $P < 0.05$). There was no statistically significant difference between the groups (the log-rank test). The final time of observation period was April 2015

LE ratio the lipiodol emulsion concentration ratio of HCC to embolized liver parenchyma

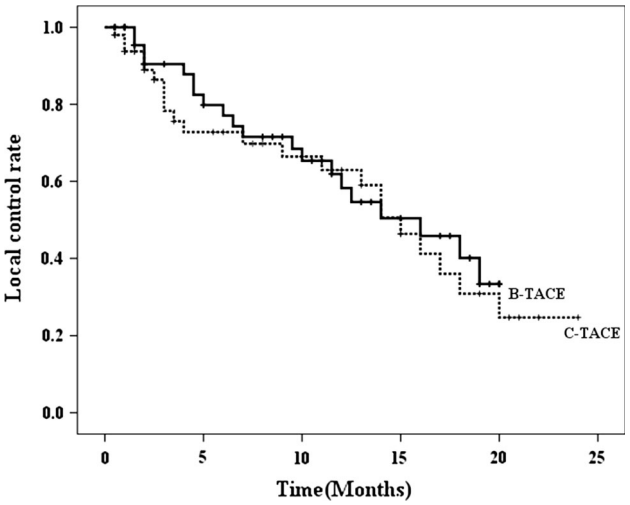

Fig. 1 Local control rate between B-TACE and C-TACE

developed severe adverse events after B-TACE had common bile duct dilatation.

Table 5 shows information about 3 patients who have the common bile duct dilatation. Cholecystectomy (in Patient No. 1), common bile duct stenosis after chronic pancreatitis (in Patient No. 2) and common bile duct stone (in Patient No. 3) were the causes. The serum bilirubin level was not elevated in all cases with biliary dilatation. Only the Patient No. 2 had increase of biliary tract enzyme (serum alkaline phosphatase: 431 IU/L; reference range: 110–340 IU/L). The remaining cases with biliary dilatation (B-TACE: $n = 4$, C-TACE: $n = 3$) had no severe adverse events.

Discussion

The present study showed that there was no statistically significant difference of the LE ratio at the level of lobar and segmental between the B-TACE group and the C-TACE group. Although a number of subsegmental cases were small, the mean LE ratio at the level of subsegmental showed a statistically significant difference between the groups (t test: $P < 0.05$). Only elevation of ALT was significantly more frequent in the B-TACE group compared with the C-TACE group (Mann–Whitney test: $P < 0.05$). However, 3 cases (6 %) of liver abscess and one case (2 %) of liver infarction were noticed in the B-TACE group, while there were no severe adverse events (liver abscess/infarction) in the C-TACE group. Although the frequency of liver abscess/infarction was higher in the B-TACE group, there was no statistically significant difference between the groups (Fisher's exact test). Our multivariate logistic regression analysis suggested that the only significant risk factor for liver abscess or infarction was bile duct biliary dilatation ($P < 0.05$).

In this study, the LE ratio at the level of lobar and segmental showed no statistically significant difference

Table 3 The adverse events

	B-TACE ($n = 50$)	C-TACE ($n = 50$)
Fever (grade 1:2:3)	20 (40 %):11 (22 %):3 (6 %)	17(34 %):12 (24 %):1 (2 %)
Abdominal pain (grade 2)	7 (14 %)	8 (16 %)
Nausea (grade 2)	14 (28 %)	9 (18 %)
Vagovagal reflex	6 (12 %)	3 (6 %)
Elevation of T-Bil (grade 1:2:3)	12 (24 %):3 (6 %):2 (4 %)	10 (20 %):5 (10 %):0
Elevation of ALT* (grade 1:2:3)	30 (60 %):9 (18 %):9 (18 %)	39 (78 %):7 (14 %):3 (6 %)
Liver abscess	3 (6 %)	0
Liver infarction	1 (2 %)	0

*Only elevation of ALT showed a statistically significant difference between the groups (Mann–Whitney test: $P < 0.05$)

ALT alanine aminotransferase, *T-Bil* total bilirubin

Table 4 Factors affecting the severe adverse events

Variable	*P* value	Odds ratio	95 % confidence interval
Patient ages	0.402	0.913	0.737–1.130
Tumor size (mm)	0.425	1.46	0.577–3.695
Lobar TACE**	0.527	4.862	0.036–656.7
Epirubicin (mg)	0.775	1.03	0.841–1.262
2nd TACE***	0.795	0.464	0.001–153.8
HbA1c (%)	0.802	1.219	0.259–5.731
Biliary dilatation	0.043*	95.14	1.148–788.3

* This study suggested that onset risk factor of liver abscess is biliary dilatation by multivariate logistic regression analysis ($P < 0.05$)

** Lobar TACE means as a TACE at the level of lobar

*** 2nd TACE means as a treatment for recurred lesion after TACE

between the B-TACE group and the C-TACE group. The B-TACE procedure and end-point of embolization used in this study, as well as the method for calculation of the LE ratio, were modified from the methods of Irie et al. [11, 13]. Irie et al. reported the LECHL ratio (the ratio of the LE concentration in the tumor to that in the embolized liver parenchyma) in patients treated by B-TACE was higher than that by C-TACE. However, that ratio was only calculated in patients with dense accumulation of LE, and they did not measure the ratio in patients undergoing C-TACE. In our study, only mean LE ratio at the level of subsegmental showed a statistically significant difference between the groups (*t* test: $P < 0.05$).

In our study, only the 1st TACE/2nd TACE ratio showed a statistically significant difference between the B-TACE group and the C-TACE group (Fisher's exact test: $P < 0.05$, 1st TACE: $n = 12$, 2nd TACE: $n = 38$ in the B-TACE group). There were many patients in the B-TACE group who received C-TACE before B-TACE. TACE may cause injury to the hepatic artery, which can lead to inflammatory stenosis and/or occlusion as a result of the irritant effect of chemotherapy agents and stagnation of blood flow caused by embolization with gelatin sponge particles. After repeated TACE, extrahepatic collaterals may provide the blood supply to the tumor [16]. Thus, restricted tumor uptake of LE due to hepatic artery stenosis and extrahepatic collateral blood supply may have resulted in no statistically significant difference of the LE ratio between the groups at the level of lobar and segmental.

Irie *et al.* analyzed the adverse events in 82 patients receiving B-TACE and reported that elevation of ALT (grade 3: 20.7 %, grade 4: 6.1 %) was significantly more frequent after B-TACE than C-TACE (grade 3: 7.5 %, grade 4: 0 %) [13]. In our study, only elevation of ALT was significantly more frequent in the B-TACE group compared with the C-TACE group (Mann–Whitney test: $P < 0.05$). A similar result may have been obtained in both studies because B-TACE causes more severe ischemia compared with C-TACE by embolization of collateral vessels.

Irie et al. reported that one out of the 82 patients (1.2 %) developed biloma after B-TACE versus four out of 161 patients (2.6 %) with biloma after C-TACE, showing no

Table 5 Three patients who have the common bile duct dilatation in The Severe Adverse Events (abscess and infarction)

Patient	Cause	Increase of biliary tract enzyme
No. 1	Cholecystectomy	–
No. 2	Common bile duct stenosis after chronic pancreatitis	+*
No. 3	Common bile duct stone	–

The serum bilirubin level was not elevated in all cases with biliary dilatation.*The serum alkaline phosphatase level was elevated (431 IU/L; reference range: 110–340 IU/L)

statistically significant difference [13]. In our study, the frequency of liver abscess after B-TACE was higher compared with their report and it only occurred in the B-TACE group. The frequency of liver abscess was also higher compared with that previously reported in patients receiving C-TACE (0.5–2.5 %) [17, 18]. Biloma after TACE seems to be a consequence of occlusion of small peripheral hepatic arteries by Lipiodol that leads to necrosis of the bile duct epithelium. In a postmortem study of patients with HCC treated by TACE, almost half of the nonnecrotic bile ducts adjacent to the necrotic ducts of bilomas demonstrated marked reduction of vascularity [19]. Lipiodol is known to occlude small peripheral hepatic vessels, especially at the level of the peribiliary capillary plexus [20, 21]. Although it was not confirmed pathologically in our study, lipiodol might have occluded the peribiliary capillary plexus more extensively after B-TACE than that after C-TACE. In our study, multivariate logistic regression analysis suggested that the significant risk factor for liver abscess/infarction was bile duct dilatation ($P < 0.05$). There is a possibility that bile duct dilatation is likely to predispose biloma formation and infection.

Therefore, B-TACE with epirubicin–lipiodol requires attention to the risk of serious complications such as liver abscess/infarction in patients who have bile duct dilatation. We found that liver abscesses tend to occur about 1 month after the B-TACE procedure, so careful follow-up is important. Although liver abscess or infarction only occurred in a small group of patients, we suggest that patients who have bile duct dilatation should not undergo B-TACE. The LE ratio at the level of subsegmental showed a statistically significant difference between the groups (t test: $P < 0.05$), so subsegmental B-TACE is more useful than C-TACE. However in biliary dilatation cases, there is a risk of abscess formation by B-TACE.

Our study had several limitations: First, it was a retrospective study performed at a single center and included a relatively small number of subjects. Therefore, our findings/conclusions should be considered preliminary, and further prospective investigation at multiple centers is required. Second, pathological examination was not performed. On CT scans, there was no statistically significant difference of the LE ratio at the level of lobar and segmental between the groups. However, the actual density of lipiodol and its residence time in the liver might have differed between the B-TACE and C-TACE groups, and such differences of lipiodol residence and/or density could have influenced the occurrence of adverse events. Pathological examination will be necessary in the future to confirm these points. Third, the pressure in the occluded artery was not measured in our study. The pressure in the occluded artery might be associated with visualization of a tumor stain during B-TACE. In other words, visualization of a tumor stain during B-TACE and C-TACE might be associated with both the efficacy and side effects of TACE.

In conclusion, the LE ratio at the level of lobar and segmental showed no statistically significant difference between the groups in the present study. Although a number of subsegmental cases were small, the LE ratio at the level of subsegmental showed a statistically significant difference between the groups (t test: $P < 0.05$). Only elevation of ALT was more frequent in the B-TACE group, showing a statistically significant difference. While B-TACE caused severe adverse events (liver abscess and infarction) in patients with bile duct dilatation, there was no statistically significant difference in incidence between the groups.

Compliance with Ethical Standards

Conflict of interest The author and co-authors have no conflict of interest to disclose with respect to this study.

Ethical approval All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in this study to the B-TACE or C-TACE procedure.

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