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Original Article

Efficacy of a microballoon catheter in transarterial chemoembolization of hepatocellular carcinoma using miriplatin, a lipophilic anticancer drug: Short-term results

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Aim: The goal of the study was to evaluate the efficacy and safety of balloon-occluded transarterial chemoembolization (B-TACE) of hepatocellular carcinoma (HCC) using miriplatin (a lipophilic anticancer drug) and gelatin particles.

Methods: B-TACE was performed for 62 HCC nodules in 33 patients who could not be treated by surgical resection or radiofrequency ablation. All 33 patients had a history of transarterial chemoembolization (TACE) treatment prior to B-TACE. As a historical comparison, we investigated 40 nodules in 28 patients treated by TACE using a conventional microcatheter (C-TACE), miriplatin and gelatin particles. The therapeutic effect per tumor was compared between the groups based on the Response Evaluation Criteria in Cancer Study Group of Japan (RECICL) and side-effects were compared based on the Common Terminology Criteria for Adverse Events (ver. 4.0).

Results: The therapeutic efficacy after 4–12 weeks was evaluated in 59 nodules in the B-TACE group and in 37 nodules in the C-TACE group. Of these nodules, TE4 occurred in 29 (49.2%) in the B-TACE group and in 10 (27%) in the C-TACE group. Local efficacy was significantly higher in nodules treated by B-TACE than by C-TACE. The side-effects on hepatic function were similar in the two groups.

Conclusion: Our results suggest that B-TACE with miriplatin is a useful treatment for hepatocellular carcinoma.

Key words: balloon-occluded transarterial chemoembolization, balloon occlusion, conventional microcatheter transcatheter arterial chemoembolization, embolization, hepatocellular carcinoma, miriplatin

INTRODUCTION

TRANSCATHETER ARTERIAL CHEMOEMBOLIZATION (TACE) is commonly used for treatment of hepatocellular carcinoma (HCC), which often shows recurrence in different regions. TACE is an important step toward molecular targeted therapy and multimodal treatment, because it is based on injection of anticancer agents into local tumor sites using a lipiodol carrier that selectively accumulates in hypervascular tumors in the liver, including in HCC nodules, coupled with occlusion of arteries by embolization. For greatest efficacy, the anticancer agent must be stably suspended in lipiodol.

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Miriplatin hydrate (MIRIPLA; Dainippon Sumitomo Pharma, Osaka, Japan) is the first lipophilic platinum agent and was approved for treatment of HCC in Japan in January 2010.[1–5] We have developed balloon-occluded transarterial chemoembolization (B-TACE) using a microballoon catheter for more efficient injection of miriplatin, compared with conventional TACE using a microcatheter (C-TACE). The goal of this study was to compare the efficacy and safety of B-TACE with those of C-TACE.

METHODS

Patients

THE SUBJECTS WERE 62 patients (101 nodules) with HCC who could not be treated by surgical resection or radiofrequency ablation. Of these subjects, 33 consecutive patients (62 nodules) underwent B-TACE with

miriplatin from September 2011 to September 2012 to treat recurrent or newly developed nodules after conventional TACE (B-TACE group). These patients were judged to need additional TACE treatment (B-TACE) unless there was an apparent tumor thrombus or intrahepatic shunt. The therapeutic effect of B-TACE was determined by contrast-enhanced computed tomography (CT) 4–12 weeks after treatment.

Patients treated with conventional TACE were chosen as a control group. However, few patients underwent conventional TACE with miriplatin during the study period, and therefore we established a historical control group of 28 patients (40 nodules) who underwent TACE with miriplatin using a conventional microcatheter from June 2010 to September 2011 (C-TACE group) (Table 1). The study was performed retrospectively after approval by the institutional ethics committee and in compliance with the Declaration of Helsinki. Written informed consent was obtained from all patients.

C-TACE and B-TACE

Transcatheter arterial chemoembolization was performed through the left upper arm using the Seldinger technique in all subjects. In the C-TACE group, a 4-Fr catheter (FANSAC IV; Terumo, Tokyo, Japan) was placed in the hepatic artery and a 1.8–2.2-Fr microcatheter was advanced through the 4-Fr catheter as close to the tumor as possible. In the B-TACE group, a 5-Fr guiding catheter (Elway; Terumo) was placed in the hepatic artery and a 3-Fr microballoon catheter (Attendant; Terumo) was advanced through the guiding catheter (Fig. 1) as close to the tumor as possible. Because the microballoon catheter was thicker than the microcatheters and could not be advanced close to the tumor in some cases, infusion of embolic agents was sometimes performed from a relatively proximal site in B-TACE.

Miriplatin (60 mg) was suspended with 3.5 cc of lipiodol and 20–120 mg of miriplatin was used per patient. One-millimeter of porous gelatin particles (Gelpart;

Table 1 Backgrounds of patients in the B-TACE and C-TACE groups

		B-TACE	C-TACE	
Number		33	28	
Age		74 (41-88)	74 (59-87)	$P = 0.376$
Sex	Male/Female	19/14	20/8	$P = 0.319$
Origin	B type-/C type +	23	18	$P = 0.825$
	B type +/C type -	0	0	
	B type +/C type +	2	0	
	B type -/C type -	8	10	
Number of tumors	1/2/3/4/≧5	13/9/5/1/5	10/6/5/1/6	$P = 0.789$
Stage	I/II/III/IVa	1/10/20/2	0/7/19/2	$P = 0.872$
Child-Pugh A/B/C		24/7/2	7/1/20	$P = 0.606$
AFP (ng/mL)		23.6 (3.7-3966)	11.8 (1.5-36463)	$P = 0.612$
AFP-L3 (ng/mL)		10.1 (0.5-66.5)	10.4 (0.5-67.7)	$P = 0.877$
PIVKA-II (mAU/mL)		27 (9-13500)	32 (9-6540)	$P = 0.643$
Frequency of MPT treatment 1/ 2/ 3/ 4/≧5		14/13/4/1/1	19/9/0/0/0	$P = 0.085$
History of local treatment Yes/No		19/14	13/15	$P = 0.605$
Frequency of TACE treatment 0		0	11	$^{*}P = 0.0004$
1-2 times		15	10	
3-4 times		9	5	
≧5 times		9	2	
Number of nodes		62 nodes	40 nodes	
Tumor size (initial treatment) (mm)		22 (7-90)	24 (10-80)	$P = 0.489$
MPT dose (initial treatment) (mg)		40 (10-120)	44 (12-120)	$P = 0.293$

Median (minimum-maximum).
B-TACE, balloon-occluded transarterial chemoembolization; C-TACE,TACE using a conventional microcatheter; *P*,*P*-value; B type, hepatitis B virus; C type, hepatitis C virus; AFP, α-fetoprotein; AFP-L3, isoform of α-fetoprotein; PIVKA-II, protein induced by Vitamin K absence or antagonists-II; MPT, miliplatin; TACE, transarterial chemoembolization.

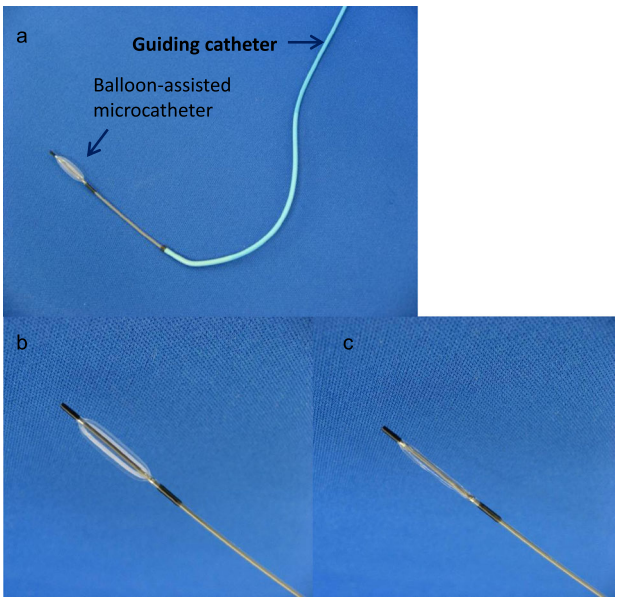


Figure 1 (a) A microballoon catheter (Attendant) inserted into a guiding catheter (Elway). (b) An expanded balloon. (c) A closed balloon.

Nippon Kayaku, Japan) and contrast agent were mixed, and these particles were fragmented into smaller sizes of 150–200 μm in length by pumping between two syringes 10 times using a three-way stopcock (as communicated by T. I. at the Japan Radiological Society Meeting, 2011). The miriplatin–lipiodol suspension was infused under balloon occlusion of the targeted vessel, followed by infusion of fragmented gelatin particles, also under balloon occlusion. After miriplatin was retained in tumors, 1-mm gelatin particles (Gelpart) were mixed with an appropriate amount of contrast agent in a 2.5-mL syringe and confirmed to be distributed in running vessels angiographically before the procedure was completed.

In B-TACE, the vasa vasorum was targeted and a catheter was injected into the subsegmental vessel in which each tumor had developed. However, the tip of a microballoon catheter is thicker than the diameter of a regular microcatheter. If the microballoon catheter did not reach the target site, it was injected from the central part. If an insufficient amount of drugs reached the tumor, a different vasa vasorum was identified by contrast-enhanced CT and drugs were injected through several vessels using a microcatheter. In B-TACE, treatment was completed when the catheter was pushed back during administration of drugs. The procedure for C-TACE was similar to that for B-TACE, except for the catheter. In C-TACE, a catheter was inserted as close as possible to the tumor, and drugs were administered. If several vessels reached the tumor, a catheter was separately inserted into each vessel and treatment was performed. C-TACE was discontinued when drugs and gelatin particles refluxed to the central region from the catheter. When drugs and gelatin particles were injected slowly but refluxed, they were injected again after several minutes. C-TACE was discontinued if reflux continued.

The objective of treatment in both groups was to inject drugs into a tumor and conduct embolization. Therefore, no tumor site or drug dose was established. The pachychromatic image before treatment was defined as the target size and gelatin particles were injected after drugs were administrated until the target size or miriplatin of 120 mg was administrated. In both groups, gelatin particles accumulated in the vasa vasorum and the operation was completed. In C-TACE, when drugs refluxed, they were injected again after several minutes; however, treatment was discontinued if the drugs continued to reflux. In B-TACE, treatment was completed when the catheter was pushed back during administration of drugs.

Imaging evaluation

Non-contrast CT was obtained immediately after B-TACE/C-TACE for evaluation of lipiodol accumulation in HCC nodules. Slices of 0.5 mm (64 rows) were collected and reprocessed into 5-mm slices. When a deficiency of lipiodol was seen in a nodule, contrast-enhanced ultrasonography was performed immediately after CT using 0.5 mL/body of an i.v. ultrasonic contrast agent (16 μL for injection; Sonazoid [Daiichi Sankyo, Tokyo, Japan]) to evaluate residual blood flow in the nodule. Coded contrast mode and coded harmonic angio mode were used in contrast-enhanced ultrasonography (LOGIQ E9; GE Healthcare, Pittsburgh, PA, USA) and the whole tumor was observed for approximately 2 min of the vascular phase after injection of the contrast agent. All nodules were visualizable by ultrasound. If a pachychromatic region was found inside the tumor, the therapeutic effect was evaluated as insufficient. In relatively large nodules, changes in the early arterial dominant phase and findings after contrast agent addition were evaluated several times.

Contrast-enhanced CT (Iomeron 350 Injection 100 mL; Eisai, Tokyo, Japan) was performed 4–12 weeks after B-TACE or C-TACE for evaluation of the treatment effect based on the Response Evaluation Criteria in Cancer Study Group of Japan (RECICL, ver. 5.12)[6] using a 64-multidector row CT system (Aquilion 64; Toshiba, Tokyo, Japan).

Safety evaluation

Common Terminology Criteria version 4.0[7] were used to evaluate adverse reactions. For safety evaluation, parameters including liver function were compared by determining temporal changes in each group after treatment. Medians for comparison of the two groups were determined from laboratory test data before the operation and 1–4 and 7 days and 2–4 weeks after treatment. Laboratory data included total bilirubin (T-Bil), aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase, γ-glutamyltransferase, alkaline phosphatase (ALP), albumin, white blood cell count (WBC), platelet count and prothrombin time ratio. Child–Pugh scores[5] before and 2–4 weeks after treatment were also compared.

Statistical analysis

The significance of differences in background parameters and efficacy data were evaluated by Fisher's exact test and Mann–Whitney *U*-test. A Wilcoxon signed rank test was used for safety evaluation and results showing multiplicity were compared by Bonferroni correction. Values of $P < 0.05$ were considered to be significant in all analyses.

Table 2 Efficacy evaluation after 4–12 weeks in the B-TACE and C-TACE groups

Local recurrence Classified into 4 grades	B-TACE Group (n=62)	C-TACE Group (n=40)	
	*		* p=0.035
TE4	29 /59 (49.2%)	10 /37 (27.0%)	
TE3+TE2+TE1	30/59 (50.8%)	27/37 (73.0%)	

Classified into 4 grades(TE1to TE4):the evaluation of treatment effect basing on Response Evaluation Criteria in Cancer Study Group of Japan(RECICL)

RESULTS

BACKGROUND FACTORS IN the B-TACE and C-TACE groups are shown in Table 1. There were no significant differences in age, sex, virus positive underlying liver disease, number of tumors, tumor stage, Child–Pugh score, tumor markers (α-fetoprotein [AFP], *Lens culinaris* agglutinin-reactive fraction of AFP%, protein induced by vitamin K absence/antagonist-II), frequency of miriplatin treatment, history of local treatment, tumor size or miriplatin dose between the B-TACE and C-TACE groups (Table 1). Only the rate of previous C-TACE treatment differed between the two groups ($P = 0.0004$).

The outcomes at 4–12 weeks after treatment in the B-TACE group were TE4 in 49.2% and TE3 to TE1 in 50.8% of the subjects, whereas those in the C-TACE group were TE4 in 27.0% and TE3 to TE1 in 73.0%. The percentage of nodules with TE4 at 4–12 weeks after treatment was significantly higher in the B-TACE group ($P = 0.035$) (Table 2).

Nodules with lipiodol accumulation of 100% or more in CT on the day after treatment were found in 67.7% of cases in the B-TACE group and 59.0% in the C-TACE group, with no significant difference between the groups ($P = 0.370$). Nodes with a complete defect in blood flow in contrast-enhanced ultrasonography were found in 64.3% of cases in the B-TACE group and 45.5% in the C-TACE group, again with no significant difference between the groups (Table 3).

Significant differences from before to after treatment were found in ALP in both groups and WBC in the B-TACE group (Table 4). Grade 3 worsening of hepatic function included increased AST in three subjects (8.2%) and increased ALT in one (3.0%) in the B-TACE group; however, all recovered 1 week after administration. T-Bil deteriorated from grade 2 before administration to grade 3 after administration in two subjects and AST increased in five subjects (17.9%) in the C-TACE group. AST recovered 1 week after administration in three of these subjects, but remained high at 4 weeks after administration in two subjects. Time-dependent postoperative changes in AST and ALT are shown in Figure 2. AST and ALT transiently increased 1–4 days after treatment, but returned to before treatment levels at 2–4 weeks in both groups.

Table 3 Efficacy evaluation using non-contrast CT and contrast enhanced ultrasonography on the day after treatment

	B-TACE Group ($n = 62$)	C-TACE Group ($n = 40$)	*P*
Non-contrast CT evaluation Percentage of complete lipiodol accumulation	42/62 (67.7%)	23/40 (57.5%)	$P = 0.370$
Contrast-enhanced US evaluation Percentage of complete lipiodol accumulation	27/42 (64.3%)	10/22 (45.5%)	$P = 0.051$

B-TACE, balloon-occluded transarterial chemoembolization; CT, computed tomography; C-TACE, transcatheter arterial chemoembolization using a conventional microcatheter; US, ultrasonography.

Table 4 Laboratory test results in the B-TACE and C-TACE groups before and 2–4 weeks after treatment

	B-TACE group			C-TACE group		
	Before administration	2–4 weeks after administration	*P**	Before administration	2–4 weeks after administration	*P**
T-Bil (mg/dL)	0.75 (0.35–1.25)	0.68 (0.29–6.34)	NS	0.71 (0.34–2.25)	0.69 (0.34–1.67)	NS
AST (U/L)	45 (23–157)	44 (25–137)	NS	48 (26–152)	53 (21–244)	NS
ALT (U/L)	27 (11–129)	27 (9–98)	NS	34 (15–133)	37 (15–180)	NS
γ-GT (U/L)	58 (13–591)	51 (15–668)	NS	60 (18–458)	58 (18–454)	NS
ALP (U/L)	341 (182–802)	381 (164–1060)	$P < 0.05$	318 (155–720)	380 (196–1043)	$P < 0.05$
LDH (U/L)	223 (161–479)	230 (165–663)	NS	236 (147–472)	221 (160–343)	NS
PT (%)	83 (47–118)	84 (28–129)	NS	82 (59–112)	80 (63–112)	NS
Alb (g/dL)	3.5 (2.7–4.5)	3.4 (2.9–4.6)	NS	3.5 (2.7–4.5)	3.4 (2.9–4.6)	NS
WBC ($\times 10^9$/L)	3.4 (1.8–6.8)	4.1 (1.4–8.4)	$P < 0.05$	4.3 (2.1–6.7)	4.5 (2–9.7)	NS
PLT ($\times 10^9$/L)	104 (24–263)	115 (24–385)	NS	120 (37–326)	125 (25–257)	NS

Values are expressed as median (minimum-maximum). C-TACE,TACE using a conventional microcatheter; B-TACE, balloon-occluded transarterial chemoembolization; *P*, *P*-value; T-Bil, total bilirubin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GT, γ-glutamyltransferase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; PT, prothrombin time; Alb, albumin; WBC, white blood cell; PLT, platelets. NS, not significant

Child–Pugh scores before and at 2–4 weeks after treatment are shown in Figure 3. The score increased by 1 or more after administration in three subjects (9.1%) in the B-TACE group and in four (14.8%) in the C-TACE group, with no significant difference between the groups. Residual liver function was similar in the two groups. Clinical findings included fever and nausea, but there were no unexpected adverse events based on the treatment criteria.

A representative case is shown in Figures 4 and 5. Lipiodol accumulation corresponding to a TE4 efficacy

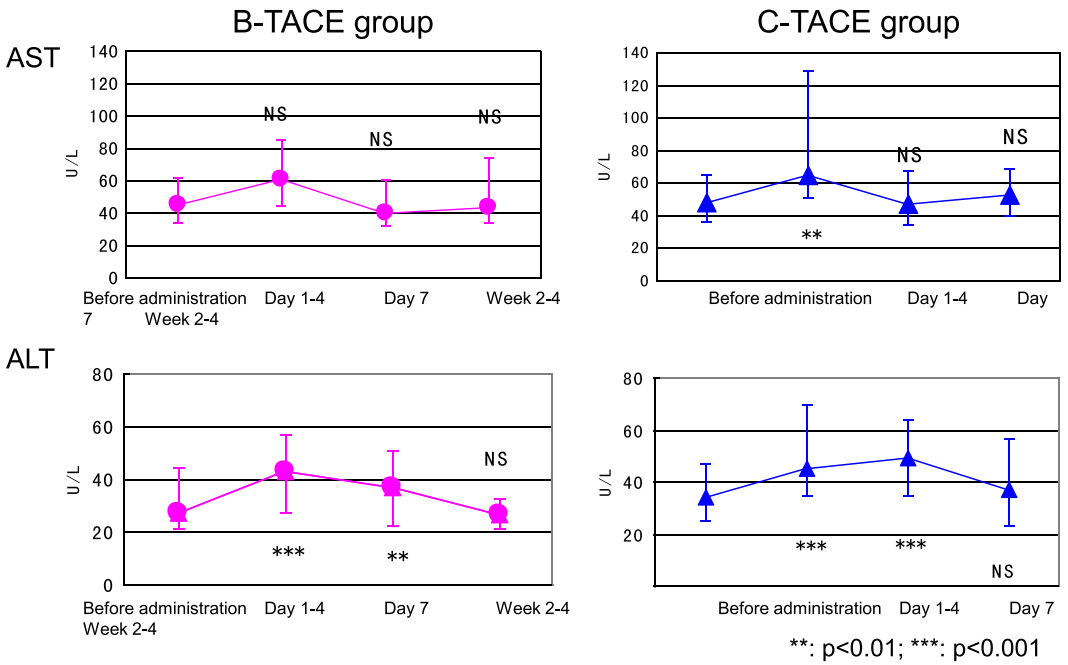
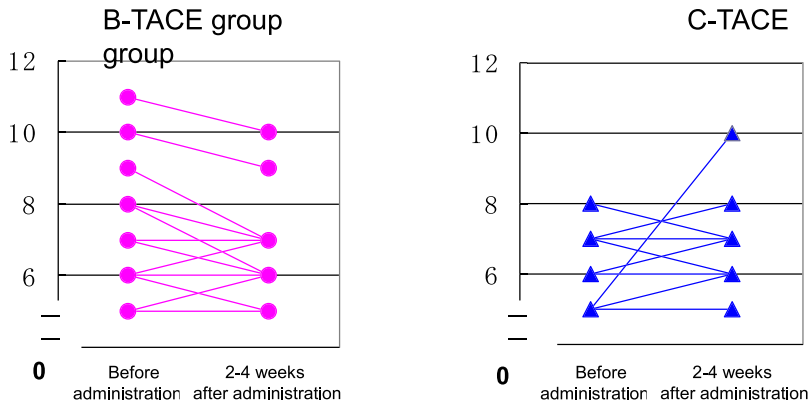


Figure 2 Time-dependent changes in serum transaminase levels after treatment in the B-TACE and C-TACE groups. AST and ALT transiently increased 1–4 days after treatment, but returned to before treatment levels at 2–4 weeks in both groups. ALT, alanine aminotransferase; AST, aspartate aminotransferase; B-TACE, balloon-occluded transarterial chemoembolization; C-TACE, transcatheter arterial chemoembolization using a conventional microcatheter.



Before administration Change (score)	B-TACE group		C-TACE group	
	Subjects	(%)	Subjects	(%)
-2	2		0	
-1	6	90.9	4	85.2
0	22		19	
1	3		3	
2	0		0	
3	0	9.1	0	14.8
4	0		0	
5	0		1	

Figure 3 Changes in residual liver function using Child–Pugh scores before and 2–4 weeks after treatment in the B-TACE and C-TACE groups. The score increased by ≥1 after administration in three subjects (9.1%) in the B-TACE group and in four (14.8%) in the C-TACE group, with no significant difference between the groups. B-TACE, balloon-occluded transarterial chemoembolization; C-TACE, transcatheter arterial chemoembolization using a conventional microcatheter.

evaluation was found in non-contrast CT on the day after treatment. However, a pachychromatic region was found in the bottom of the tumor in contrast-enhanced ultrasonography on the day after treatment and a pachychromatic region was found in the bottom of the tumor in contrast-enhanced CT 1 month after treatment; thus, the case was evaluated as TE3 (Fig. 4). Local recurrence in the same case was retreated with B-TACE (Fig. 5). B-TACE was performed through almost the same vessel, but the cystic artery is involved in Figure 4 while an embolus in this branch is avoided in Figure 5. Efficacy was evaluated as TE4 until 12 months after treatment with no local recurrence.

DISCUSSION

MANY PATIENTS WITH HCC have hepatic cirrhosis as an underlying disease. These patients are likely to have poor residual liver function and may not be indicated for molecular-targeted drugs or local treatment due to recurrence in different regions. Therefore, TACE for HCC has an important role as multimodal treatment. New embolizing agents including beads for vascular embolization, which are used to permanently block blood flow, have been developed for hepatic artery embolization and treatment options are increasing.[8–14] Peripheral devices and catheters for transarterial treatment have similarly improved. Our replacement of a conventional catheter with a microballoon catheter permits performance of B-TACE with miriplatin. In the current study, we examined the efficacy of this procedure for treatment of recurrent HCC.

Grüntzig *et al.* described procedures for using a balloon inside vessels in angioplasty and first applied this to practice in 1974.[15] Flexible balloons were developed for the abdomen and used for arterial injection and balloon-occluded retrograde transvenous obliteration.[16] Nakamura *et al.* used this approach for treatment of HCC in 1985.[17] Irie *et al.* proposed B-TACE using a microcatheter in 2009 and performed treatment using a 6-Fr guiding catheter. A microcatheter with an attached balloon inserted into a

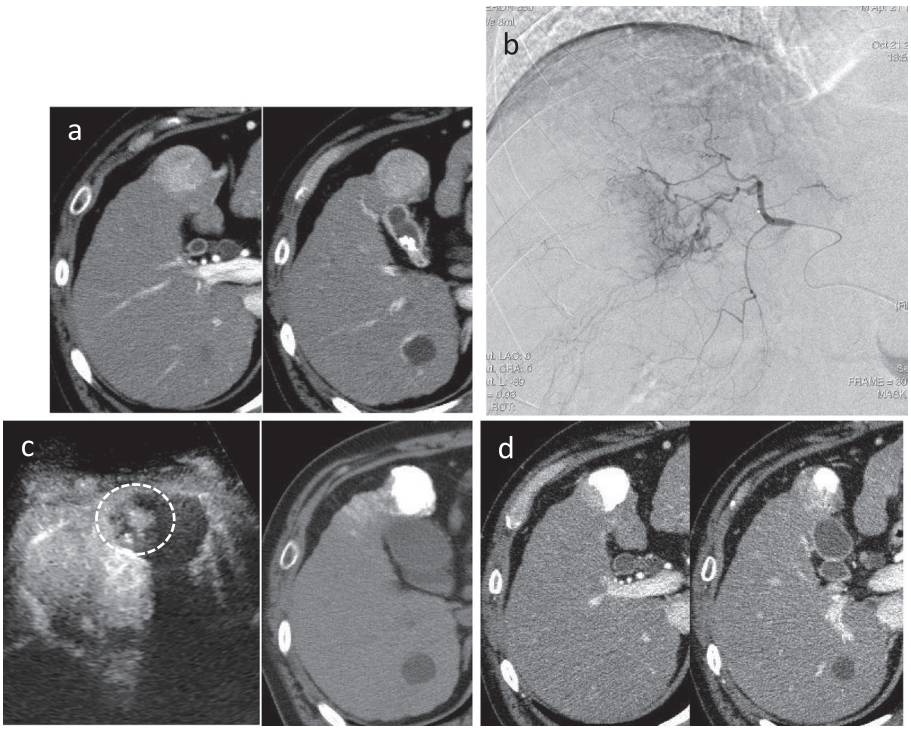


Figure 4 A case of S5 hepatocellular carcinoma (30 mm in diameter) treated using conventional TACE. (a) Uniform pachychromatic images in tumors in the arterial dominant phase in contrast-enhanced CT before treatment. (b) Angiography of the right hepatic artery was followed by TACE performed by inserting the catheter into the cephalic vein. (c) Contrast-enhanced ultrasonography on the day after treatment showing a pachychromatic region in the bottom of the tumor, and a non-contrast CT image on the day after treatment showing lipiodol accumulation corresponding to a TE4 efficacy evaluation. (d) Arterial dominant phase in contrast-enhanced CT 1 month after treatment, showing local recurrence. CT, computed tomography; TACE, transcatheter arterial chemoembolization.

5-Fr guiding catheter was approved in 2011 and B-TACE has now been performed in several institutions, along with reduced puncture size and improved balloon performance for reaching peripheral vessels. Irie *et al.* showed that intravascular pressure on the tumor side of a balloon was decreased by occluding the central artery, which is the vasa vasorum in HCC, using a microballoon.[18,19]

Injection of agents using a balloon for artery occlusion on the central side may cause leakage of the agents into the portal vein and the hepatic parenchyma due to compression, leading to incidental diseases. In patients with HCC with abundant arterial blood, intravascular pressure inside tumors decreases; therefore, injection of agents with use of a balloon to reduce blood flow on the central side can increase intravascular pressure and direct the agents to tumors using the pressure slope. Therefore, it is important not to over-expand a balloon or compress agents unnecessarily because B-TACE can facilitate administration using the hemodynamics of HCC. Intravascular pressure in non-neoplastic sites decreases under balloon occlusion as contrast agent flows into growing tumor vessels; consequently, lipiodol remains static and is inhibited from flow into normal cells. After balloon release, lipiodol occluded in arteries of non-neoplastic sites outflows into the portal vein via normal arteries, causing earlier release of artery occlusion and relatively prompt release of agents in non-neoplastic sites.

Miriplatin is a platinum-containing agent that is highly effective against HCC, similarly to epirubicin, doxorubicin and mitomycin C, which are commonly used in TACE. Miriplatin is converted to dichloro(1,2-diaminocyclohexane)platinum *in vivo* and forms platinum-DNA cross-links through covalent bonds with DNA strands in cancer cells.[1,2] Miriplatin is more lipophilic than conventional platinum-containing agents and can be stably suspended in lipiodol, which should promote accumulation in HCC cells and support a sustained-release antitumor effect.[3,4] These properties make it an ideal drug for use in B-TACE. There are few studies comparing the effects of C-TACE using conventional agents and miriplatin, but TE4 evaluations of 20–40% have been reported at 1–3 months after treatment.[20–25] The reasons for failure

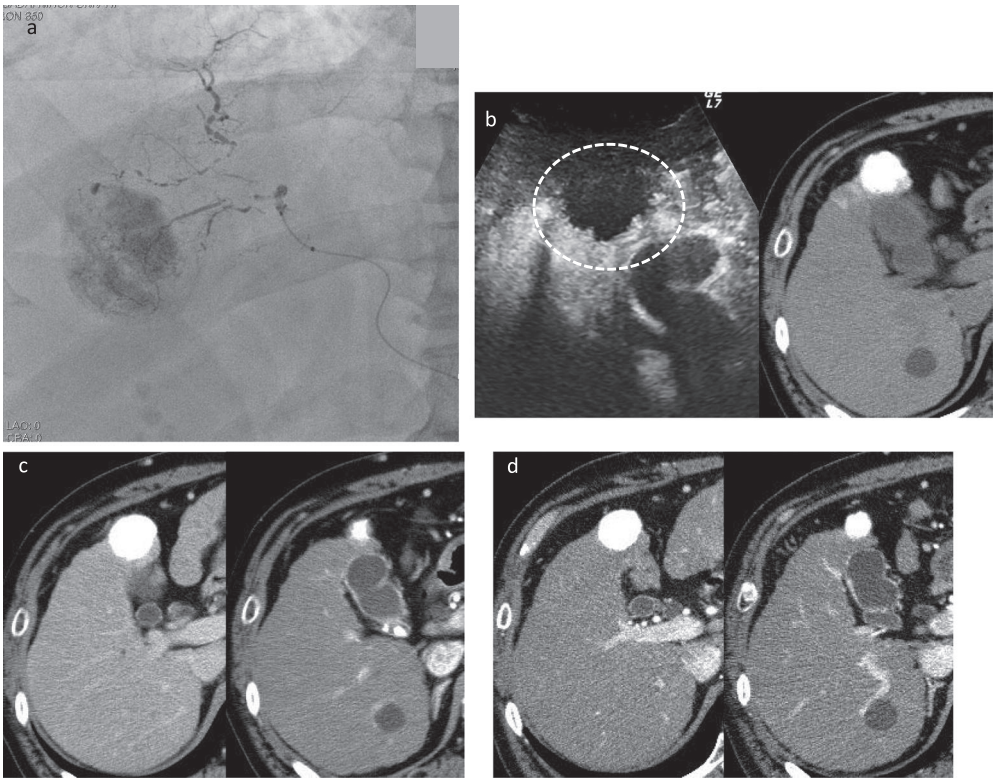


Figure 5 A case of hepatocellular carcinoma (the patient in Fig. 4) treated using B-TACE for local recurrence. B-TACE was performed slightly on the central side compared with the previous treatment. (a) Angiography of the right hepatic artery. (b) Contrast-enhanced ultrasonography on the day after treatment and a non-contrast CT image on the day after treatment showing lipiodol accumulation corresponding to a TE4 efficacy evaluation. (c) Arterial dominant phase in contrast-enhanced CT 1 month after treatment, showing no local recurrence. (d) Arterial dominant phase in contrast-enhanced CT 4 months after treatment, also showing no local recurrence. B-TACE, balloon-occluded transarterial chemoembolization; CT, computed tomography; C-TACE, transcatheter arterial chemoembolization using a conventional microcatheter.

include insufficient lipiodol suspension reaching the tumor due to viscosity and limited release due to insufficient embolization. New procedures for injecting miriplatin include warming to decrease viscosity,[26–28] which does not require replacement of the catheter.

The distribution of miriplatin suspension in non-contrast CT on the day after treatment showed no significant difference between B-TACE and C-TACE in this study. However, more nodules with defect regions of 100% or more, which corresponded to a TE4 evaluation, were present after B-TACE, although without a significant difference compared with C-TACE. Contrast-enhanced ultrasonography is highly sensitive to blood flow and unlikely to be affected by lipiodol;[29–35] therefore, this result suggests that fine blood flow in tumors was suppressed earlier in B-TACE. The increased inhibition of blood flow in the B-TACE group may be an important reason for the greater efficacy of B-TACE in determination of the therapeutic effect at 4–12 weeks after treatment. Also, B-TACE was performed in more recurrent cases and had disadvantages including poor peripheral access due to the end-attached balloon. Despite this situation, B-TACE was highly effective. In comparison with C-TACE with a microcatheter, B-TACE is a useful procedure and probably reduces differences between operators, which is a problem in C-TACE. Thinner catheters have also been developed and B-TACE is an option without use of a guiding catheter such as that used in conventional angiography. Matsumoto *et al.* described a 1.8-Fr tip microballoon catheter enables selective catheterization in patients with HCC and B-TACE using the 1.8-Fr tip microballoon catheter is a safe procedure.[36]

Miriplatin is an anticancer agent that produces less vascular disease including narrowing vessels and shunt formation and only transiently remains in vessels surrounding tumor vessels, and thus has no major side-effects.[37–39] No significant change in surrounding vessels was found in retreatment after C-TACE (Fig. 5) and no marked defects

of normal vessels were found in retreated subjects. Therefore, B-TACE had no major effects on normal vessels. There were no significant difference in the effects on hepatic function between B-TACE and C-TACE, which indicates that B-TACE is at least as safe as C-TACE. There is likely to be an increase in elderly patients and in the number of patients with poor residual liver function, and effects on hepatic function will be an important factor in choice of treatment in these patients.

We note that miriplatin is only available in Japan and was only approved 5 years ago. Therefore, more studies of B-TACE with miriplatin are needed to establish this treatment for HCC. However, the study shows that B-TACE significantly increased the local effect of miriplatin. B-TACE may allow anticancer drugs to be administrated from the central side more extensively in comparison with C-TACE. In addition, this study suggests that B-TACE using miriplatin with hepatic artery embolization is more effective than C-TACE for treatment of HCC, with no difference in adverse effects on hepatic function between the two procedures.

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