Chapter 5　Transcatheter Arterial Chemoembolization (TACE)

- **Introduction**

Typical hypervascular hepatocellular carcinoma (HCC)　is nourished by arteries. Consequently, a useful treatment method known as transcatheter arterial embolization (TAE) has come to be commonly used. In TAE, a catheter is used to inject embolic material into the hepatic arteries that provide nourishment for the tumors (feeding arteries), resulting in obstruction of the feeding arteries and consequent ischemic necrosis of the tumor.

Until the early 1990s, embolic material was injected after arterial infusion of anticancer drugs; alternatively, a mixture of embolic material and anticancer drugs was injected into the tumor feeding arteries. Thereafter, a method known as transcatheter arterial chemoembolization (TACE) that was characterized by the accumulation of iodized oil (Lipiodol®) within tumors was developed. In this method, a mixture of Lipiodol® and an anticancer drug (lipiodol emulsion) was injected into the tomor feeding arteries, followed by injection of embolic material.

Until the mid-1990s, the majority of unresectable, hypervascular HCCs were treated with TACE/TAE. With the introduction of percutaneous local therapies, such as radiofrequency ablation (RFA), TACE/TAE is currently indicated for unresectable, hypervascular HCC that cannot be treated with percutaneous local therapy.

In the 2000s, two reports of a randomized controlled trial (RCT) and meta-analysis using Lipiodol® have proven that Lipiodol® with TACE/TAE (Lip-TACE/TAE) contributes to an improved prognosis for unresectable HCC.

However, the definitions of catheter-based intra-arterial therapies such as TACE/TAE are not universal, and this often creates difficulties when comparing the results of reports. In this section, therefore, we have evaluated catheter-based intra-arterial therapies according to the "General Rules for the Clinical and Pathological Study of Primary Liver Cancer (5th revised and expanded edition)," as shown below.

1. Transcatheter arterial infusion (TAI): Hepatic arterial injection of anticancer drugs without embolic material. We noted whether Lipiodol® was concurrently used or whether or not a reservoir was used. Injection of lipiodol emulsion alone was indicated as "Lip-TAI". It should be noted that this method is referred to in many reports as "chemoembolization" or "TACE".
2. TAE: Obstruction of arteries using gelatin sponge particles, porous gelatin particles, Ivalon, and other solid, spherical embolic materials, but not anticancer drugs.
3. TACE: A chemoembolization therapy that uses anticancer drugs and solid embolic materials [gelatin sponge particles, porous gelatin particles, Ivalon, or the recently developed drug-eluting beads (DEB), etc.]. In particular, the most commonly used procedure worldwide is Lip-TACE, which uses gelatin sponge particles or porous gelatin particles to induce embolization after injection of a lipiodol emulsion.

CQ37 Who are eligible for TACE/TAE?

Recommendation

TACE/TAE is a recommended treatment for unresectable hypervascular HCC in patients with Child–Pugh class A or B liver disease who are contraindicated for percutaneous ablation. Selective TACE/TAE takes into consideration the residual liver functional reserve and the ratio between the volume of healthy liver to be chemoembolized and the total volume of healthy liver; therefore, it is recommended **(Grade A)**.

Although TACE/TAE is reportedly useful in patients with intravascular tumor thrombus(particularly portal vein tumor thrombus) and no extrahepatic metastasis, evidence to make a formal recommendation is insufficient **(Grade C1)**.

- **Scientific Statement**

HCCs whichare indication of TACE/TAE show dense tumor staining on hepatic angiography; the

tumors in such cases as referred to as hypervascular HCC (LF06687[1] Level 4, LF10451[2]). In Japan, most patients with unresectable HCC are treated with TACE/TAE. Nevertheless, there are no RCTs supported by high-level scientific evidence that studied TACE/TAE and its effects on prognosis; furthermore, the techniques are not standardized.

In the late 1990s, five non-Japanese RCTs that compared patients with advanced HCC treated with TACE/TAE with those treated with symptomatic treatments were reported (LF02313[3] Level 1b, LF02332[4] Level 1b, LF02745[5] Level 1b, LF02959[6] Level 1b, LF03734[7] Level 1b). Antitumor effects [tumor shrinkage, decreased alpha fetoprotein (AFP) levels, decreased incidence of portal vein tumor thrombus, etc.] were reported in all studies, although TACE/TAE did not contribute to improvement in prognosis. In the early 2000s, however, two RCTs reported that TACE/TAE positively influenced the aforementioned antitumor effects and survival rate compared with symptomatic treatment (LF01899[8] Level 1b, LF06283[9] Level 1b).

In 2008, the results of the large-scale RCT, SHARP study (LF12054[10] Level 1b), which examined treatments for unresectable, advanced HCC, led to the establishment of sorafenib as a standard therapy for advanced HCC. As a result, TACE/TAE became indicated only for HCC patients with 4 or more tumors, Child–Pugh class A or B, a performance status (PS) of 0–2, and stage B (intermediate stage; L3H00018[11]). Therefore, TACE/TAE may also be indicated for HCC patients with Child–Pugh class A or B liver damage who cannot undergo surgery or percutaneous ablation therapy (including patients with extrahepatic metastasis and severe vascular invasion).

Emergency TAE for patients with ruptured HCC is a useful treatment to control bleeding from HCC since TAE is less invasive compared with surgery (LF06783[12] Level 4).

- **Explanation**

TACE/TAE is a standard treatment method in Japan that is essential for treating unresectable, advanced hypervascular HCC with dense tumor stain on hepatic angiography, which cannot be treated with percutaneous ablation therapy (LF06687[1] Level 4, LF10451[2]). As stated previously, the antitumor effects of TACE/TAE were confirmed by RCTs in the 1990s; however, these RCTs

consistently showed no contribution to survival rate (LF02313[3] Level 1b, LF02332[4] Level 1b, LF02745[5] Level 1b, LF02959[6] Level 1b, LF03734[7] Level 1b).

In the early 2000s, 2 RCTs reported that TACE/TAE improved the prognosis of advanced HCC (LF01899[8] Level 1b, LF06283[9] Level 1b). Both reports excluded Okuda class III or Child–Pugh class C patients, and RCTs from the 2000s included chemoembolization using a selective catheterization technique, which result inless noncancerous tissue damage compared with RCTs from the 1990s. Cammà et al. performed a meta-analysis of 18 studies and found that the overall 2-year mortality rate was significantly lower in the TACE/TAE group than in the nontreatment group (odds ratio: 0.54, 95% confidence interval: 0.33–0.89, p = 0.015). However, their result had not provedn that TACE is more effective than TAE (LF01920[13] Level 1a). Cammà et al. have also stated that TACE/TAE methods (whether treatments should be scheduled regularly or not, catheter selectivity, and drugs used) and the degree of tumor progression (tumor number and tumor diameter) should be standardized to the fullest extent possible in RCTs of TAE/TACE. Since 2005, there has not been no report with a high level of evidence that discusses inclusion criteria of TACE/TAE therapy in a homogenous study population. It is therefore recommended that nonselective TACE/TAE should be avoided and that TACE/TAE should be excluded in patients who show poor liver function such as Okuda class III and Child–Pugh class C, as accordance with the exclusion criteria used in the aforementioned RCT in which TACE/TAE improved the prognosis of advanced HCC.

Indication of TACE/TAE treatment stated by initial study of the BCLC group (LF10451[2]) were as follows, (1) stage B (intermediate stage), 4 or more nodules, Child–Pugh class A or B, Okuda class I or II, PS 0–2 or (2) stage C (advanced stage), PS 1 or 2, portal vein invasion (−), N1 (−), M1 (−). This was nearly identical to the indications of TACE/TAE described in the 2005 and 2009 editions of the guidelines (LJ10001[14], LJ20001[15]), i.e., patients with 2 or 3 tumors larger than 3 cm in diameter or 4 or more tumors (size irrelevant) (LF10451[2], LF10686[16] Level 6) with Child–Pugh class A or B liver disease. This was followed by the release of the results of the

large-scale SHARP study in 2008 that examined unresectable, advanced HCC (LF12054[10] Level 1b), sorafenib was determined to be the standard treatment for advanced HCC. Therefore, according to the guidelines of the Society of Interventional Radiology (SIR) in the United States and the revised American Association for the Study of Liver Diseases (AASLD) guidelines of the BCLC group, TACE/TAE is indicated only for patients with 4 or more tumors and Child–Pugh class A or B, PS 0–2, and stage B (intermediate stage) (L3H00018[11]).

Many studies reported that TACE/TAE is contraindicated in patients with intravascular tumor thrombosis (particularly portal vein tumor thrombus) (LF10451[2]). However one study showed thatpatients of severely advanced cancer with mild liver dysfunction (patients with intravascular tumor thrombus or those with giant HCCs measuring 10 cm or larger) achieved long-term survival using a combination of TACE/TAE with other therapies (LF10262[17] Level 2a). In addition, among the aforementioned RCTs in which TACE/TAE contributed to the improvement in advanced HCC prognosis, the one study reported that portal vein tumor thrombus was present in 9 out of 40 patients in the Lip-TACE group and 12 out of 39 patients in the control group; therefore, the clinical efficacy of TACE/TAE is undeniable for stage C (advanced stage) patients with intravascular thrombus (particularly portal vein tumor thrombus) without extrahepatic metastasis. However, because there are no reports with a high level of evidence comparing TACE/TAE with standard therapy with sorafenib, the efficacy of TACE/TAE against intravascular tumor thrombus is unclear.

In the previously mentioned RCT, TACE/TAE was contraindicated for advanced HCC in patients with a PS of 3 or higher, older age (75–80 years or older), complications of decompensated cirrhosis (gastrointestinal bleeding, refractory ascites, hepatic encephalopathy, bacterial infection), severe coagulopathy, and renal disorders, among other factors (LF02313[3] Level 1b, LF02332[4] Level 1b). Recent reviews have also mentioned portal vein occlusion, hepatofugal portal blood flow, encephalopathy, recent bleeding from esophageal varices, refractory ascites, portal-systemic shunt, and extrahepatic lesions are contraindication of TACE/TAE (L3F00101[18] Level 6).

According to Takayasu et al., two large-scale, prospective cohort studies pertaining to factors contributing to an improvement in the prognosis of Lip-TACE (use of Lipiodol emulsion and gelatin sponge particles) for unresectable HCC were conducted on a nationwide scale by the Liver Cancer Study Group of Japan (LF10462[19] Level 2a, L3H00021[20] Level 2a). A study reviewing 8,510 patients from 1994 to 2001 revealed that Lip-TACE was safe for unresectable HCC and resulted in a 5-year survival rate of 25% and that independent prognostic factors for Lip-TACE included the degree of liver damage, stage classification, and AFP levels (<401 ng/mL or ≥401 ng/mL). A recent study reviewing 4,966 patients from 2000 to 2005 revealed that the 5-year survival rate increased to 34% and that the degree of liver damage, stage classification, AFP levels, and PIVKA-II levels were independent prognostic factors for Lip-TACE. This report clearly demonstrated the treatment outcome of TACE, which was included as a treatment option in the 2005 edition of the Clinical Practice Guidelines for Hepatocellular Carcinoma. Furthermore, outcomes were found to be significantly different between the TACE and non-TACE groups (surgical resection or local therapy), and it was demonstrated that the TACE recommendations in the guidelines represented a valid treatment strategy.

Future issues regarding TACE/TAE therapy for advanced HCC include, as mentioned earlier, the efficacy of TACE/TAE for BCLC stage C (advanced stage) patients with intravascular tumor thrombus (particularly portal vein tumor thrombus) without extrahepatic metastases and the efficacy of combination therapies with molecular target drugs, especially sorafenib. However, although several clinical studies are in progress at this time, their results have not been released. Meanwhile, DEB may become available for use, even in Japan, and these may, in turn, lead to the development of new treatment possibilities. Regarding the treatment effect of DEB, a randomized phase II trial (PRECISION V) comparing DEBs-TACE with Lip-TACE (L3F00064[21] Level 2a), showed the usefulness of DEBs-TACE, which is being used in western countries. However, DEBs-TACE is currently in the phase II trial, thus we must await further developments to determine whether DEBs-TACE has the potential to replace Lip-TACE as a standard therapy and

investigate the different applications of DEBs.

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CQ38 What type of embolic material or anticancer agent should be used in TACE/TAE?

Recommendation

Lipiodol TACE (Lip-TACE) using Lipiodol® is recommended when performing TACE/TAE. Sensitivity to anticancer agents varies among cases, and a specific drug that can be used as an anticancer agent in a Lipiodol® emulsion has not been established. In Japan, porous gelatin spherical beads (Gelpart®; particle diameter of 1 or 2 mm) are available as the embolic material **(Grade C1)**.

- **Scientific Statement**

Iodized oil (Lipiodol®) characteristically gets trapped within the tumor (tumor sinusoid) and surrounding liver sinusoids. Lipiodol® acts as a drug delivery system when mixed with anticancer drugs. When a lipiodol emulsion is injected into the hepatic arteries, the emulsion retained within the tumor and it allows for the controlled release of the entrapped anticancer drug (LF06687[1] Level 4, LF06881[2] Level 2a).

Survey results of an annual average of 4,774 liver cancer treatments, performed between 2002 and 2004 at 17 institutions in Japan, showed that Lipiodol® was used in more than 90% patients with TACE; therefore, Lipiodol® is generally used for TACE in Japan (L3F00237[3] Level 6). When performing TACE, anticancer drugs such as epirubicin, doxorubicin, mitomycin C, cisplatin, and neocarzinostatin can be used in lipiodol emulsions (LF02651[4] Level 4, LF03653[5] Level 1b, LF03756[6] Level 2a, LF04041[7] Level 4, LF06299[8] Level 4, LF06881[9] Level 2a). Combination chemotherapies using these anticancer drugs are used in many facilities; however, there are no reports verifying the superiority of any specific drug.

A cisplatin-based drug (IA-call®) with increased solubility has been used in CDDP/lipiodol suspensions for hepatic arterial infusion chemotherapy in patients with unresectable, advanced HCC. Although the usefulness of this treatment has been frequently reported, none of the reports are supported by high-level evidence (L3F00188[10] Level

It has been reported that TACE performed with a CDDP/lipiodol suspension and porous gelatin particles for embolization yields superior treatment effects compared with hepatic arterial infusion chemotherapy without embolization (L3F00265[12] Level 2a). Some comparisons of TACE using a CDDP/lipiodol suspension with TACE using a doxorubicin/lipiodol suspension have also shown that the effects of treatment are significantly better with CDDP (L3F00186[13] Level 2b, L3F00267[14] Level 2b), whereas no significant differences were observed in a different report (L3F00235[15] Level 1b).

Miriplatin (Miripla®) is a lipophilic platinum agent that easily forms a suspension with Lipiodol®

and has recently become available for clinical use. Reports regarding its efficacy (L3F00223[16] Level 2b, L3F00177[17] Level 4) have emerged, and the development of future research is anticipated.

Gelatin sponge particles have been conventionally used as the embolic material in TACE/TAE for HCC (LF03080[18] Level 1b). Porous gelatin particles (particle diameter 1 and 2 mm: Gelpart®) are a type of spherical embolic material that are sterile and standardized and were approved by the National Health Insurance in 2006. Thereby, intravascular administration of another gelatin sponge particles (Spongel®) was contraindicated in October of that same year. Moreover, although porous gelatin particles (Gelpart®) may be used in TACE/TAE for HCC, they must not be used in TACE/TAE of other organs or for diseases other than HCC (LJ10002[19], LJ10004[20] Level 4). At this time, no other spherical embolic material is approved for hepatic arterial administration in Japan, except the porous gelatin particles mentioned above.

TACE using Lipiodol® and gelatin sponge particles was compared with hepatic arterial infusion chemotherapy using Lipiodol® without gelatin sponge particles, and opinions regarding the survival rate were divided; it was significantly increased with TACE in one report (L3F00250[21] Level 2a), whereas no increase was reported in another (L3F00224[22] Level 1b).

- **Explanation**

In recent years, with advancements in imaging devices, such as catheters, guidewire systems, and CT angiography, it has become possible to identify the branches of arteries that supply the tumor and superselectively insert catheters into the branches. As a result, it has become possible to superselectively inject large amounts of chemoembolic material into not only the hepatic arteries but also the portal vein branches through tumor sinusoids (LF06687[1] Level 4, LF10291[23] Level 4). Furthermore, these advancements in catheter insertion technology have made it possible to inject high concentrations of anticancer drugs into the tumor area and induce ischemia in both the arteries and portal vein. As a result, the effects of anticancer treatment have improved, and liver function can be preserved in noncancerous liver tissue, showing that TACE/TAE markedly

improves prognosis (LF06299[8] Level 4, LF06687[1] Level 4, L3F00281[24] Level 3, L3F00144[25] Level 3). However, HCC tumors located between liver segments or on the surface of the liver have multiple feeding vessels that include collateral blood flow from outside the liver; therefore, the incidence of local recurrence is high (LF10291[23] Level 4, LF10830[26] Level 2b). Although good survival rates have been reported often with TACE/TAE using superselective catheters, there are no studies that provide high-level evidence (LF10804[27] Level 6, LF10451[28] Level 6).

Patients with advanced HCC and good liver function and those with small HCC have a favorable post-treatment prognosis with Lip-TACE, and histopathological examination performed for resected specimens using the same procedure show strong antitumor effects (LF02959[29] Level 1b, LF06604[30] Level 2a). The survival rate using Cox's proportional hazard model is significantly different between Lip-TACE and TACE ($p < 0.01$; LF06604[30] Level 2a). However, no meta-analysis has shown better survival rates with TACE than with TAE in patients with advanced HCC (LF01920[31] Level 1a). This was probably because Lip-TACE in RCT was performed on nearly the entire liver; therefore, damage to noncancerous liver tissue may have been a major factor for the decreased survival rate (LF01920[31] Level 1a).

In one RCT, survival rates after two different types of anticancer agents (epirubicin vs. doxorubicin) were used in lipiodol emulsions and injected with gelatin sponge particles during Lip-TACE therapy (LF03653[5] Level 1b) were investigated. No differences in adverse effects were observed between the two drugs, and survival rates were good with doxorubicin in the low-risk group ($p = 0.018$). However, no overall difference was observed between the outcomes of the two treatments. In terms of the survival rates of embolization therapy (with gelatin sponge particles) after injection of lipiodol emulsions using low-dose cisplatin and doxorubicin (31% cisplatin, 50% doxorubicin), the survival rate with cisplatin was significantly higher than that with doxorubicin ($p < 0.05$; LF06324[32] Level 2b).

From August 2006, spherical porous gelatin particles (particle diameters 1 and 2 mm: Gelpart®) were approved by the National Health Insurance in Japan for use as an embolic material in

TACE/TAE. Since then, these spherical porous gelatin particles have been used in the vast majority of TACE/TAE procedures performed for HCC in Japan till date. The short-term results of one study found no major differences in treatment effects or incidence of adverse effects between TACE/TAE using porous gelatin particles (Gelpart®) and that using gelatin sponge particles (Spongel® or Gelform®) (LJ10004[20] Level 4).

In recent years, a variety of spherical embolic materials have been developed mostly outside of Japan, using various raw materials such as acrylic, polyvinyl alcohol (PVA), and gelatin (L3F00077[33] Level 2b, L3F00126[34] Level 1b, L3F00226[35] Level 4). Currently, in addition to spherical embolic material, drug-eluting beads (DEBs) have been developed and are used for the treatment of HCC because they can easily be loaded with drugs for controlled release. Anticancer drugs that are loaded onto DEB (doxorubicin) remain in high concentrations within the tumor, and pharmacokinetic analysis has shown that the drug does not flow into the peripheral circulation. Short-term results have also shown that this method is highly effective and has few adverse effects (L3F00126[34] Level 1b). Lip-TACE using a lipiodol emulsion containing doxorubicin was compared with TACE using DEB, and although the results were favorable compared with those of Lip-TACE, no significant differences were observed (L3F00064[36] Level 1b, L3F00233[37] Level 1b). Resected specimens obtained after liver transplantation for HCC showed that the tumor necrosis rate was significantly higher with DEB-TACE than with conventional TAE (L3F00086[38] Level 3).

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CQ39　How should repeat TACE/TAE be scheduled?

Recommendation

Repeat TACE/TAE should be performed if a tumor develops with ample blood flow, if tumor marker levels are elevated, or if the tumor diameter has increased **(Grade B)**.

- **Scientific Statement**

In 1991, Ikeda et al. reported that TAE performed regularly once every 3 months was effective, and complete necrosis was achieved with continuously repeated TAE (LF06751[1] Level 4). This was followed by several reports of RCTs that investigated patients with advanced HCC who were regularly treated with TACE/TAE every 2–3 months or with symptomatic treatment. These studies were published in highly reputed journals and became the focus of much discussion (LF02313[2] Level 1b, LF02332[3] Level 1b, LF02745[4] Level 1b, LF02959[5] Level 1b, LF03734[6] Level 1b). Although the results of these five RCTs confirmed the aforementioned antitumor effects, it was concluded that therapy did not contribute to prolong survival rates. On the other hand, recent results of repeated superselective TACE performed for restricted patients with tumor growth have shown 3-year survival rates of 78% and 77.1% (LF06299[7] Level 4, LF06687[8] Level 4). Studies of post-treatment recurrence have also reported that repeated TACE extends the survival duration (L3F00306[9] Level 4). In addition, repeated radiotherapy combined with TACE may extend survival time in patients with portal vein tumor thrombosis and preserved liver function (L3F00054[10] Level 4).

- **Explanation**

Institutions that perform repeated TACE/TAE in response to tumor growth or elevated tumor marker levels often achieve good survival rates (LF05818[11] Level 2b, LF10804[12] Level 6). Nevertheless, there have been no RCTs comparing the effects of regular, short-term repeated TACE/TAE performed every 2–3 months with repeated TACE/TAE performed only in response

to increased tumor growth (LF10686[13] Level 6).

Ernst et al. performed at least 3 regular sessions of Lip-TACE therapy once every 2 months and retrospectively compared the results with those of Lip-TACE performed only when further tumor growth was observed (LF05818[11] Level 2b). In their results, complications occurred more frequently with the former treatment strategy than with the latter ($p < 0.001$); consequently, the cumulative survival rate was poorer with the former ($p < 0.001$). The authors have stressed the importance of performing superselective Lip-TACE when tumor growth is observed.

Reviews on the literature from 2002 onward showed that repeat TACE/TAE was often recommended in cases of tumor growth (LF10295[14] Level 6, LF10451[15] Level 6, LF10686[13] Level 6, LF10804[12] Level 6, L3F00101[16] Level 6). In addition, there is a test for determining the pros and cons of repeated TACE that utilizes a prognostic scoring system based on risk factors associated with repeated TACE (L3F00283[17] Level 4).

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CQ40 What types of diagnostic imaging techniques are useful for evaluation of the treatment effect of TACE?

Recommendation

Dynamic CT or dynamic MRI is recommended **(Grade B)**.

- **Scientific Statement**

CT is internationally recognized as the first-line imaging procedure for determining the efficacy of

TACE. When Lipiodol® CT is performed, if Lipiodol® is completely deposited in the lesion, necrosis is observed in 98% of the lesion, and if deposition is incomplete, necrosis is observed in 64% of the lesion. Therefore, the treatment outcome of TACE can be determined by the Lipiodol® deposition pattern (LF06743[1] Level 3).

With the use of dynamic CT, evaluateion of blood flow in the tumor region allows the identification of residual lesions or recurrence of HCC after TACE. However, there are certain limitations to the use of CT for evaluating the effect of TACE. If Lipiodol® deposition in the tumor is incomplete, differentiating between contrast media enhancement and Lipiodol® deposition becomes difficult, and if Lipiodol® deposition affects hemodynamics in the lesion area, it is difficult to identify tumor staining (LF10937[2] Level 1).

The efficacy of dynamic MRI for assessing the treatment effect of TACE has been reported since the 1990s (LF06572[3] Level 3, LF05932[4] Level 3). When dynamic CT was compared with dynamic MRI, CT tended to underestimate residual lesions (L3F00195[5] Level 1), and liver transplantation studies have shown that MRI is more sensitive and specific than CT (L3F01994[6] Level 2a). A comparison study of lipiodol CT, power Doppler ultrasound, and dynamic MRI has shown that MRI is superior in terms of sensitivity, specificity, and diagnostic accuracy (LF01932[7] Level 1). Tumor staining in dynamic MRI performed 1 month after TACE was highly correlated with a recurrent lesion found 6 months after TACE. These results suggest that recurrence can also be predicted using MRI findings (L3F00050[8] Level 3).

In recent years, several reports have demonstrated the usefulness of diffusion-weighted MRI for evaluation of the tumor in the body. However, liver transplantation studies have shown that dynamic MRI is superior to diffusion-weighed MRI for evaluating complete necrosis in a lesion (L3F00212[9] Level 1), and studies predicting post-TACE recurrence have found no significant difference between lipiodol CT and diffusion-weighed MRI (L3F00290[10] Level 1). The combined use of diffusion-weighted imaging and dynamic MRI enhances the sensitivity of detecting recurrence after TACE; however, the specificity is decreased and the diagnostic accuracy is

unchanged (L3F03426[11] Level 3). Therefore, the marked efficacy of diffusion-weighted imaging has not been demonstrated till date.

- **Explanation**

Generally, evaluation result of TACE treatment may influence the subsequent treatment planning of the HCC.

Although the serum AFP level is an HCC tumor marker, recurrence often occurs after TACE despite normal AFP levels. Therefore, evaluation by imaging is important for determining the treatment outcome.

Dynamic CT is generally used to determine the effects of TACE therapy; however, in addition to the previously stated reasons, high-attenuation and beam-hardening artifacts caused by Lipiodol® deposition may make it difficult to evaluate local recurrence.

Whereas, on MRI, Lipiodol® does not interfere with lesion visualization, and residual lesions may be visualized as enhanced areas if contrast agents are used. High-speed three-dimensional dynamic imaging methods, which have become widely available in recent years and can be used to acquire thin-section images that match those obtained with CT, eliminating partial volume effects and enabling the acquisition of extremely small staining areas. Another benefit of MRI is the lack of exposure to ionizing radiation. Although diffusion-weighted images do not currently appear to be particularly useful, there have been remarkable technological advances in this imaging modality, and there is the additional benefit of not requiring contrast agents. Therefore, further studies are likely to be performed in the future.

Although there are several advantages in MRI, it is unrealistic to assess the treatment outcome of TACE using MRI in all patients, because of the higher cost and/or longer examination time compared to CT. CT is useful enough for determining the clinical treatment outcome of HCC after TACE. Therefore, dynamic CT and dynamic MRI are both recommended in these guidelines.

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