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• *BRIEF REPORTS* •

The value and limitation of transcatheter arterial chemoembolization in preventing recurrence of resected hepatocellular carcinoma

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Abstract

AIM: To evaluate the value and limitation of postoperative transcatheter arterial chemoembolization (TACE) in preventing recurrence of hepatocellular carcinoma (HCC).

METHODS: In the first group, 987 postoperative patients with HCC, who did not have any evidence of recurrence in the first preventative TACE but were found to have recurrence at different times during the follow-up survey, were analyzed. In the second group, 643 postoperative patients with HCC had no TACE for compared study. To study the relationship between the recurrence time and the number of TACE treatments was analyzed.

RESULTS: The 6-, 12-, and 18-mo recurrence rates in the first and second groups were 22.2% (210 cases) *vs* 61.6% (396 cases), 78.0% (770 cases) *vs* 74.7% (480 cases) and 88.6% (874 cases) *vs* 80.1% (515 cases). There were significant differences between the recurrence rates of the two groups at 6 mo ($P<0.0001$).

CONCLUSION: The principal role of TACE after HCC operation is to suppress, detect early and treat micrometastasis. It has a good effect of preventing recurrence of HCC in 6 mo, but such an effect is less satisfactory in a longer period. When it is uncertain whether HCC is single-central or multi-central and if there is cancer residue or metastasis after operation, TACE is valuable to prevent recurrence.

Key words: Liver neoplasm; Prevent recurrence; Therapy; Resection

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INTRODUCTION

The 5-year postoperative recurrence rate of hepatocellular carcinoma (HCC) is 60%. Transcatheter arterial chemoembolization (TACE) is usually performed to prevent recurrence, but up to now there has been no report of large case capacity about its outcome. We studied 1 630 postoperative cases of HCC, whether they had undergone TACE or not, and analyzed the value and limitation of postoperative TACE in preventing recurrence of HCC.

MATERIALS AND METHODS

Patients

Study group: Between June 1996 and June 2001, 3 781 patients with HCC confirmed by surgery and pathology underwent preventative TACE treatment, from whom, we selected 987 patients who had no demonstrable evidence of residual disease on the first angiographs, but experienced recurrence at different times of the follow-up period as the study group.

Control group: Six hundred and forty-three patients with HCC, who did not receive TACE after hepatectomy and experienced recurrence in the follow-up period, were selected as the control group.

Timing of interventional therapy

TACE was performed by DSA (Adventx EX, GE, USA) in all cases. If the routine celiac or hepatic artery angiography showed no explicit recurrence, the first preventative TACE was performed by injecting emulsion epirubicin hydrochloride mixed with 3-5 mL iodized oil in the appropriate hepatic artery, with or without addition of 10 mg hydroxycamptothecin. If recurrence foci were detected in later follow-up and TACE treatment, the dosage of antitumor drugs and iodized oil was determined by the number, size, blood supply and liver function. Otherwise, the dose was similar to the first time.

The first TACE treatment was performed usually 1-2 mo after the operation, and the second TACE treatment was carried on 3-5 mo after the first one. Whether more TACE therapy was needed depended on the finding of follow-up US or CT imaging.

Determination of recurrence time

Recurrence time was counted by months from the operation date to the first time that recurrence was found, regardless of how many preventive TACE therapies had been performed for the patient. As for the control group, it was counted from the operation date to the date when recurrence was confirmed by any re-check.

RESULTS

Study group

No evidence of recurrence was found in the first angiography. There were 219 patients (22.3%) who had viable cancer tissue detected in the 2nd TACE, 289 (29.3%) in the 3rd, 262 (26.5%) in the 4th, 105 (10.5%) in the 5th and 113 (11.5%) in later than 5th therapy. The 6- and 12-mo recurrence rate was 22.3% (219 patients) and 78.0% (770 patients) respectively. The 6- and 12-mo disease-free rate was 77.8% (768 patients) and 21.99% (217 patients), respectively.

Control group

The 6- and 12-mo recurrence rate was 61.6% (396 patients) and 74.7% (480 patients) respectively. The 1-, 2-, and 3-mo recurrence rate was 10.1% (65 patients), 21.0% (135 patients) and 13.2% (85 patients) respectively. The 6- and 12-mo disease-free rate was 38.4% (247 patients) and 25.3% (163 patients), respectively (Table 1).

Statistical analysis

There were conspicuous discrepancies between the study and control groups in recurrence and non-recurrence (χ^2-test, χ^2 = 1 462.725 and 299.0122, P<0.0001). There were statistically significant differences between the two groups during 6 and 18 mo (χ^2-test, χ^2 = 257.229 and 22.106, P<0.0001).

DISCUSSION

The high metastasis rate and recurrence rate are main factors that affect HCC prognosis. It is reported that the 5-year recurrence rate of HCC patients who received surgical intervention is 60%, and it is higher than 40% in small HCC patients who received radical resection. The recurrence mainly happened 2 years after operation[1,2] and the peak is at half or 1 year[3]. It is generally accepted that long-term recurrence is primarily from multi-center growth of the tumor, and short-term recurrence is from the intrahepatic metastatic haplocenter that was not excised thoroughly. Tumor cells and tissue could be dispersed into liver tissue or blood circulation by press and crush in the operating process. There may also be tiny lesions that are not detected by preoperative or intraoperative examination. So, almost all HCC have recurrence probability in theory.

At the present time, TACE is the main preventative postoperative treatment. However its curative effect is of much debate. Some researchers reviewed the literature from 1980 to 1999 and came to the conclusion that adjuvant therapy had no evident efficacy when they compared the TACE group with the control group[4]. Having studied two series of patients (68-case and 49-case) respectively, other researchers considered that TACE was effective in prevention of recurrence and promotion of survival , and it was reported that 6- and 12-mo recurrence rate was 1.5% and 5.9% in the 68-case group study[5]. However, Ono *et al*.[6], studied 108 cases and concluded that, whether the patients had chemotherapy or not, there was no obvious difference in the survival rate.

Surgeons usually believe that tumors with daughter nodules, portal vein tumor thrombi or without evident envelops could not be totally resected and preventative TACE should be performed 1-2 mo after operation. For tumors that are limited with evident envelope and have no tumor thrombi, monthly follow-up is indicated.

We[7] reported 142 patients who had no preventative TACE and recurred after operation, where the 6- and 12-mo recurrence rate was 69.7% and 83.8% respectively, and the peak of recurrence was in 6 mo. In this study, the 6-mo recurrence rate was 22.2% (219 patients), which was much lower than the control group (61.6%). And the 12-mo recurrence rate was comparable (78% *vs* 74.7%). The statistic results indicate that the peak of recurrence was postponed to 6-12 mo, while in the control group it was within 6 mo. Although the effect of TACE is definite in preventing postoperative recurrence within the first postoperative 6 mo, it seems that TACE is unable to prevent recurrence completely and its long-term effect of preventing recurrence is limited. The recurrence rate of the control group was even lower than that of the treatment group after 18 mo.

The metastasis and recurrence pathogenesis of HCC are not perspicuous at present. It is likely that the tumor cells penetrate surrounding vessels by chemotaxis, adhering, dissolving matrix and basilar membrane, and disperse from portal vein system, and become new foci by inducting vessel formation after they arrive at some place. Simple postoperative TACE treatment cannot disturb or arrest the movement of tumor cells in any step above but embolize micro-vessels of little lesions in existence that cannot display on images yet. TACE helps in controlling micro intrahepatic metastasis that remains after surgical removal of mono-center HCC, but is almost useless for multi-center HCC; therefore, the efficacy is limited. However, postoperative TACE can discover recurrence earlier and help timely healing[8].

Both artery and vein feed HCC. Therefore, the therapy for tumor cells in the portal vein system, which cannot be solely achieved by TACE, must be given much attention. Some researchers pointed out that treatment directed at the hepatic artery and portal vein at the same time could depress the postoperative recurrence rate.

In conclusion, the chief functions of postoperative TACE

Table 1 Recurrence time of TACE group and control group

	Study group (987 patients)				Control group (643 patients)			
Recurrence time (mo)	6	12	18	>24	6	12	18	>24
Recurrence cases	219	770	874	987	396	480	515	643
Recurrence rate (%)	22.2	78.0	88.6	100	61.6	74.7	80.1	100
Disease-free cases	768	217	113	0	247	163	128	0
Non-recurrence rate	77.8	22.0	11.4	0	38.4	25.3	19.9	0

are restraining micro tumors, which transmitted or were not cut off, preventing recurrence, also discovering and treating them earlier, but such functions are limited in preventing multi-center tumors. Although the preventive efficacy of TACE is limited after 6 mo, when it is uncertain whether the cancer is multi-central or mono-central and there is remnant or micro metastasis, postoperative TACE is still necessary and can obviously postpone the recurrence time.

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