Comparison of therapeutic effectiveness of combined interventional therapy for 1126 cases of primary liver cancer

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INTRODUCTION

Transcatheter arterial interventional therapy is extensively used in treating hepatocellular carcinoma (HCC). To reduce the intra-hepatic recurrence and improve the protective efficacy after treatment for HCC, some scholars have proposed combined interventional therapy as a choice of treatment for HCC[1]. We analyzed the therapeutic effectiveness of different combined interventional therapies for HCC according to the survival rate, liver function, image data and indications of tumor.

MATERIALS AND METHODS

Patients
A total of 1126 patients were retrospectively studied from January 1994 to October 2003. Of them, 873 were males and 253 were females (aged 32-76 years, mean 56.2 years). The patients were treated following the HCC Clinical Diagnosis and Staging Standard stipulated at the 8th National Academic Conference of Liver Cancer in September 2001. Among these patients, 78 had a family history of liver cancer, 985 had a medical history of serum hepatitis, 48 had a medical history of hepatitis C, 342 had cardinal symptoms of right upper quadrant pain, 336 felt epigastric distention after dinner or suffered from anorexia, 162 had low fever accompanied with progressing wasting, 286 exhibited no overt symptoms. Prior to the treatment, AFP was greater than 20 ng/mL in 735 cases, greater than 400 ng/mL in 521, negative in 227, unknown in 164. A total of 874 patients were followed up for 2

Abstract

AIM: To verify the effect of combined interventional therapy for hepatocellular carcinoma (HCC).

METHODS: The clinical data of 1126 HCC patients who received combined interventional therapy for transcatheter arterial chemoembolization (TACE) before or after hepatectomy, TACE and radio-frequency ablation (RFA), Chinese medicine treatment and biotherapy after TACE or transcatheter arterial infusion (TAI), were reviewed according to the results of their liver function, alpha-fetoprotein, image data, color-urosonography finding and survival rate.

RESULTS: A total of 874 patients were followed up for a period of 2 to 63 mo. The overall 1-, 3- and 5-year survival rates were 67.8%, 28.7% and 18.8% respectively. The 1- 3- and 5- year survival rates of patients who received TACE were 74.7%, 41.4%, 36.9% before hepatectomy and 78.9%, 40.4%, 37.5% after hepatectomy. The effective rate (PR + NC) after TACE and RFA was 93.4%, the 1- and 3- year survival rates were 74.5% and 36.8% after TACE and RFA. The effective rate of PR + NC after TACE was 83.2%. The 1-, 3- and 5- year survival rates were 69.3%, 21.7%, 8.4% after TACE. The effective rate of PR + NC after TAI was 27.5%, the 1- and 2- year survival rates were 11.6% and 0% after TAI. The liver function, color-urosonography finding and alpha-fetoprotein after TACE + RFA, TACE and TAI were compared. There was no significant difference in each index between TACE and RFA or TACE and TAI as well as in liver function between TACE and RFA or between TACE and TAI.

CONCLUSION: The therapeutic effectiveness of TACE before or after hepatectomy is most significant, while the effect of TACE and RFA is better than that of TACE, and the effect of TAI is minimal.

Key words: Hepatocellular carcinoma; Transcatheter arterial chemoembolization; Combined interventional therapy; Survival analysis
Table 1 Clinical data of 1126 patients

| Group                | Total | Preop. TACE | Postop. TACE | TACE + RFA | TAI | Total |
|----------------------|-------|-------------|--------------|------------|-----|-------|
| n                    | 1126  | 258         | 154          | 126        | 119 | 1126  |
| Karnofsky scores     |       |             |              |            |     |       |
| (n)                  |       | 20-145      | 93           | 104-154    | 153 | 0     |
| HBsA (+)             |       |             |              |            |     |       |
| (n)                  |       | 5-10        | 10-15        | 15-20      | 20-25| 0     |
| AVF                  |       |             |              | (h)        |     |       |
| (n)                  |       | 3           | 5-7          | 7-10       | 10-12| 12    |
| Embolus in PV        |       |             |              |            |     |       |
| (n)                  |       | 3           | 5-7          | 7-10       | 10-12| 12    |

Table 2 Clinical data of 1126 patients

| Group                | Total | Preop. TACE | Postop. TACE | TACE + RFA | TAI | Total |
|----------------------|-------|-------------|--------------|------------|-----|-------|
| n                    | 1126  | 258         | 154          | 126        | 119 | 1126  |
| Karnofsky scores     |       |             |              |            |     |       |
| (n)                  |       | 20-145      | 93           | 104-154    | 153 | 0     |
| HBsA (+)             |       |             |              |            |     |       |
| (n)                  |       | 5-10        | 10-15        | 15-20      | 20-25| 0     |
| AVF                  |       |             |              | (h)        |     |       |
| (n)                  |       | 3           | 5-7          | 7-10       | 10-12| 12    |
| Embolus in PV        |       |             |              |            |     |       |
| (n)                  |       | 3           | 5-7          | 7-10       | 10-12| 12    |

to 63 mo (averaged 26.3 mo). Combined interventional therapy was given, including transcatheter arteria hepatica chemoembolization (TACE) before or after hepatectomy, radio-frequency ablation (RFA) after TACE, Chinese medicine treatment and biotherapy after TACE or transcatheter arteria hepatica infusion (TAI). The clinical data of various kinds of combined interventional therapy for HCC are shown in Tables 1 and 2.

**TACE**

Twelve mg mitomycin (MMC) and 1.0 g 5-FU were diluted in 60 mL sodium chloride solution respectively and infused through a catheter. Then 50 mg epirubicin (EPI) and iodinated oil were compounded into a mixed emulsifier and infused into the blood-supply artery of the tumor through a catheter. Then, the artery was embolized with granules of spongia gelatinosa.

**TAI**

Fifty mg EPI, 12 mg MMC, and 1.0 g 5-FU were diluted in 60 mL sodium chloride solution respectively and infused through a catheter into the blood-supply artery of tumor. HCC patients treated 3-4 times with TACE at 1-2 mo intervals after hepatectomy, if pathological report showed remnant cancer cells on the cutting edge or AFP > 20 ng/mL or the image showed remnant tumor. Those who lost the chance of one-stage operation were treated with TACE + RFA, TACE and TAI were categorized into 4 degrees: complete remission (CR), partial remission (PR), no change (NC) and progression (PD). The first 3 degrees were considered efficient and the last degree was considered inefficient.

**Follow-up**

The liver and renal function, AFP, blood RT, KPS scores were re-examined, and sonography, CT, chest X-Ray were performed once a month, and then every 3 mo during the follow-up period. The date on which the patients lost their follow-up was regarded as the date of death. According to the WHO evaluation standard of therapeutic effect of solid tumor (1981), the patients who were treated with TACE + RFA, TACE and TAI were categorized into 4 degrees: complete remission (CR), partial remission (PR), no change (NC) and progression (PD). The first 3 degrees were considered efficient and the last degree was considered inefficient.

**Statistical analysis**

SPSS12.0 was used for statistical analysis. The survival rate was evaluated by adopting probability ratio multiplication theorem, and chi-square test was used for comparison between the 2 groups. P < 0.05 was considered statistically significant.

**RESULTS**

A total of 874 cases were followed up for 1-7 years. Comparison of the accumulated survival rate after various kinds of combined interventional therapy is shown in Table 3. The therapeutic effect of interventional therapy in 562 patients is shown in Table 4. Changes of liver function, tumor blood-supply and AFP in 562 cases after interventional therapy were compared. Fifteen days after combined interventional therapy, color Doppler was used to detect the blood flow around and inside the tumor. The change in recovery rate of AFP before and after TACE + RFA, TACE and TAI was compared. The results are shown in Table 5.
DISCUSSION

At present, hepatectomy remains the preferred method to treat primary liver cancer. Second-stage hepatectomy after TACE is a great breakthrough in the field of liver cancer treatment after hepatectomy of macro-hepatoma in the 1950-1960s and micro-hepatoma in the 1970s[3]. TACE after radical excision of hepatoma can efficiently kill remnant cancer cells, decrease recurrence and increase survival rate remarkably[3,5]. However, it was reported that TACE can damage hepatic and immunologic function, thus deceasing the survival rate[5]. Zheng et al[5] retrospectively analyzed the therapeutic results of 420 HCC patients after combined therapy, and found that the 1- and 3-year survival rates of non-angioencroached HCC patients after treated with TACE are 100% and 60% before radical excision, 77.8% and 22.2% before palliative excision, respectively, higher than those of the patients not treated with TACE before hepatectomy, and there is no significant difference between TACE before and after hepatectomy. Wang et al[7] reported that the 1-, 3-, 5- year survival rates of 20 HCC patients after treated with combined therapy are 95.0%, 63.5%, 32.9% after second-stage hepatectomy, suggesting that the 1-, 3-, 5- year survival rates after TACE before or after hepatectomy are the highest. The reasons may be as follows: some of the 1126 cases treated with TACE before or after hepatectomy had hepatic AVF and embolus of hepatic portal vein, only interventional therapy was given before hepatectomy; and TACE treatment did not continue with double-chemoembolization or internal radiation. All these indicate that cancer cells can extend to distal ramulus along homonymous portal vein during operation procedures. Though macroscopic circumscription of hepatoma is satisfactory, there are remnant cancer cells on the cutting edge, and liver cancer complicating hepatic cirrhosis limits circumscription of hepatectomy. The above-mentioned factors are the major reasons for recurrence which is an important reason for the low survival rate after hepatectomy. For this reason, it is necessary to treat HCC patients with TACE combined with Chinese medicine and biotherapy to increase their immunologic function after hepatectomy. To effectively increase the survival rate, HCC patients should be treated with double-chemoembolization or internal radiation before hepatectomy.

Combined interventional therapy including TACE, TAI, RAF, percutaneous intra-tumor absolute alcohol injection (PEI), percutaneous intra-tumor acid injection (PAAI), percutaneous intra-tumor hot saline water injection (PSI), percutaneous cryotherapy (PCT), is dominantly used in non-surgical treatment of HCC. Except for TACE and TAI, extra-hemal and circumscriptus “interstitial substance therapy”[9] can treat HCC through different mechanisms. It was reported that chemoembolization can reduce the number of newly generated tumor vessels and the remnant tumor may generate new vessels through various ways[9]. To increase the life span, we believe that HCC patients should be treated with RAF, PEI, PAAI, PSI, and PCT on the basis of TACE to kill remnant cancer cells. Liu et al[9] reported that the 1-, 2-, 3- year survival rates of HCC patients after treated with TACE are 59.52%, 22.06% and 14.34%, while the 1- and 3- year survival rates of HCC patients after treated with TAI are 27.94% and 0%. In our study, the 1-, 2-, 3- year survival rates of 387 patients after treated with TACE were 69.3%, 21.7% and 8.4% respectively, and the 1- and 3- year survival rates of 69 after treated with TAI were 11.6% and 0%, suggesting that combined interventional therapy for HCC is influenced by many factors.

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