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Percutaneous Microwave Coagulation Therapy for Hepatocellular Carcinoma

Toshimasa ASAHARA[1], Hideki NAKAHARA[1], Toshikatsu FUKUDA[1], Tamaki NAKATANI[1], Masatsugu YANO[1], Hiroshi HINO[1], Yuzo OKAMOTO[1], Koji KATAYAMA[1], Toshiyuki ITAMOTO[1], Eiji ONO[1], Kiyohiko DOHI[1], Mikiya KITAMOTO[2] and Toshio NAKANISHI[2]

1) Department of Surgery II, Hiroshima University School of Medicine, Kasumi 1–2–3, Minami-ku, Hiroshima 734–8551, Japan
2) Department of Internal Medicine I, Hiroshima University School of Medicine

ABSTRACT

We evaluated the efficacy of percutaneous microwave coagulation therapy (PMCT) as compared with hepatectomy in 19 patients with hepatocellular carcinoma (HCC). In 6 patients with tumors more than 3cm in diameter, coagulation was inadequate after a single session of PMCT. Patients with multiple tumors had recurrence within 1 year. For single tumors 3cm or less in diameter, the therapeutic effectiveness of PMCT was comparable to that of hepatectomy in cumulative survival and cancer-free survival rates. We conclude that PMCT should be used in the initial treatment of HCC only in patients with single tumors of up to 3cm in diameter. Surgical removal is recommended for tumors of more than 3cm in diameter.

Key words: *Hepatocellular carcinoma, Microwave coagulation*

Microwave coagulation is very useful for hemostasis and has been used clinically to resect parenchymal organs, such as the liver and spleen.

Hepatic surgery with the use of a microwave tissue coagulator, first described by Tabuse in 1979, has been shown to have excellent hemostatic and coagulation-promoting properties.

Recently, percutaneous microwave electrodes have been developed and used under ultrasonic guidance to treat liver tumors locally.

Since 1994 our department has used microwave coagulation therapy (MCT) to treat not only small hepatic tumors, but also large unresectable hepatic tumors.

In this article, we describe our clinical experience with percutaneous microwave coagulation therapy (PMCT) in the management of HCC.

PATIENTS AND METHODS

Patients

We studied 19 patients with HCC who underwent PMCT at our department between June 1994 and November 1997. The reasons for selecting PMCT were rejecting hepatectomy, complicating severe pulmonary dysfunction and failure of percutaneous ethanol injection therapy (PEIT).

The study group had an age of 63.4 ± 11.2 years, and comprised 13 men and 6 women. HCC was located in various segments of the liver, except for S1. Twelve patients had single tumors, and 7 had multiple tumors. All but one patient had a history of hepatitis B or C. The indocyanin green retention rate at 15 min (ICG R-15) was very high (34.6 ± 16.8%), indicating advanced liver diseases. Tumor markers were positive in 5 patients: AFP was more than 100 ng/ml in 4, and PIVKA-II was more than 0.1 Au/ml in 1.

The patients were divided into two groups: 13 with a maximum tumor diameter of 3cm or less, and 4 with a maximum tumor diameter of more than 3cm. The response to treatment in these groups was compared with the response to surgery in 110 patients with HCC who underwent partial hepatectomy at our department during the study period. The age of these patients was 60.9 ± 8.4 years. There were 82 men and 28 women. Eighty-three patients had single tumors, and 27 had multiple tumors. The maximum tumor diameter was 3cm or less in 68 patients, and more than 3cm in 42.

PMCT Procedure

Patients assigned to PMCT underwent a tumor biopsy with a 21 G biopsy needle, performed under local anesthesia. The biopsy needle was inserted via a subcostal or an intercostal approach with the patients in a supine position. After biopsy, a 14 G

Address for reprint requests: Toshimasa Asahara, Department of Surgery II, Hiroshima University School of Medicine, Kasumi 1–2–3, Minami-ku, Hiroshima 734–8551, Japan
TEL: +81–82–257–5221, FAX: +81–82–257–5224

guide needle was inserted near the tumor. The inner needle was removed, and a 1.6mm PMCT needle was inserted into the tumor. A feeding current (60 watts × 30 sec per irradiation) was applied to induce coagulation. On average, the PMCT regimen was as follows: 102.9 ± 59.3 sec in a single puncture for tumors 20mm or less in diameter, 218.9 ± 123.7 sec in 1 to 3 punctures for tumors 21 to 30mm in diameter, and 441.2 ± 189.4 sec in 1 to 7 punctures for tumors 31 to 40mm in diameter. The liver was examined by computed tomography (CT) about a week after the end of treatment to verify that there was no residual tumor.

Table 1. Characteristics of patients who underwent PMCT or hepatectomy with a tumor of 3cm or less

	PMCT (n=13)	hepatectomy (n=68)
male: female	7:6	50:18
age	61.9±11.6	60.5±8.5
tumor size	21.9±5.5	20.5±6.1
single: multiple	11:2	57:11
positive HCV ab	10	36
positive HBsAg	0	17
total bilirubin	1.6±0.8	0.9±0.4 *
prothronbin time	70.9±19.2	91.3±28.9 **
ICG R-15	33.8±13.8	19.9±12.4 **

* p<0.05 compared with PMCT,
** p<0.01 compared with PMCT

Table 2. Characteristics of patients who underwent PMCT or hepatectomy with a tumor of more than 3cm

	PMCT (n=6)	hepatectomy (n=42)
male: female	6:0	32:10
age	66.8±9.4	61.6±8.1
tumor size	40.3±11.0	43.7±14.9
single: multiple	1:5	26:16
positive HCV ab	6	30
positive HBsAg	0	3
total bilirubin	1.8±1.4	0.9±0.4
prothronbin time	52.9±19.1	85.9±26.3 *
ICG R-15	36.6±23.1	19.8±8.5 **

* p<0.05 compared with PMCT,
** p<0.01 compared with PMCT

Statistical Analysis

The statistical significance of differences among the groups was assessed by t-test. Survival was calculated by the Kaplan-Meier method and compared by the log-rank test.

RESULTS

The demographic characteristics of patients whose tumors had a maximum diameter of 3cm or less were compared in the PMCT group and the hepatectomy group. Although there was no significant difference between the groups in sex, age, mean tumor diameter, single-to-multiple-tumor ratio and associated hepatitis virus infection, the total bilirubin level, prothrombin activity (PT) and ICG R-15 value differed significantly, indicating that baseline liver function was better in the hepatectomy group (Table 1). Among patients whose tumors had a maximum diameter of more than 3cm, the PMCT group and the hepatectomy group were similar with respect to sex, age, mean tumor size and single-to-multiple-tumor ratio. Baseline PT activity was significantly better in the hepatectomy group, although the difference was not as obvious as that in patients with tumors of 3cm or less in diameter (Table 2).

Table 3. Outcome of patients treated by PMCT with a tumor of 3cm or less

No.	Age/sex	location	tumor size (mm)	recurrence	prognosis (month)
1	30M	S8	10	–	36, alive
2	69F	S3	16	–	32, alive
3	66M	S3	17	13 months, S3	32, alive
4	46F	S2	23	10 months, S2	17, died
5	67M	S8	28	35 months, S8	35, alive
6	67M	S7	29	–	28, alive
7	58M	S8	18	–	25, alive
8	66M	S4	29	22 months, S4	23, alive
9	62M	S8	25	–	22, alive
10	64F	S3	20	–	11, alive
11	79F	S7	22	–	1, alive
12	68F	S3	23	8months, multiple	17, alive
		S3	15		
		S8	21		
		S7	19		
		S3	27		
13	62F	S3	21	9 months, multiple	19, died
		S7	23		

* location: S; segment

Table 4. Outcome of patients treated by PMCT with a tumor of more than 3cm

No.	Age/sex	location	tumor size (mm)	recurrence	prognosis (month)
14	70M	S6	33	–	9, alive
15	62M	S5	14	12 months, S3, S6	13, alive
		S6	31		
16	76M	S4	36	7 months, multiple	13, died
		S6	25		
		S8	32		
17	65M	S2	25	7 months, multiple	9, died
		S4	20		
		S4	22		
		S8	52		
		S8	44		
18	50M	S5	30	5 months, S8	7, alive
		S5	13		
		S8	31		
19	78M	S8	59	7 months, multiple	12, alive
		S8	12		

* location: S; segment

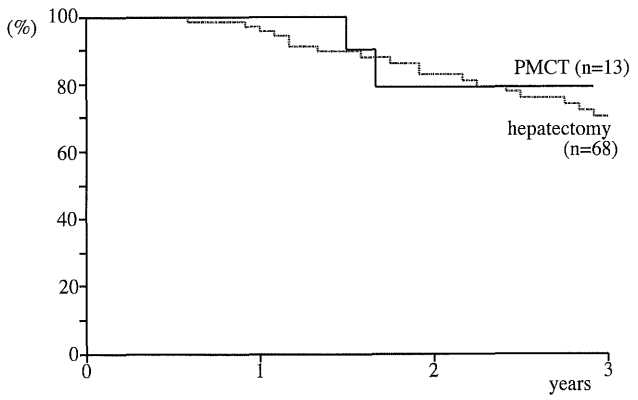

Fig. 1. Cumulative survival of patients who underwent PMCT or hepatectomy with a tumor of 3cm or less

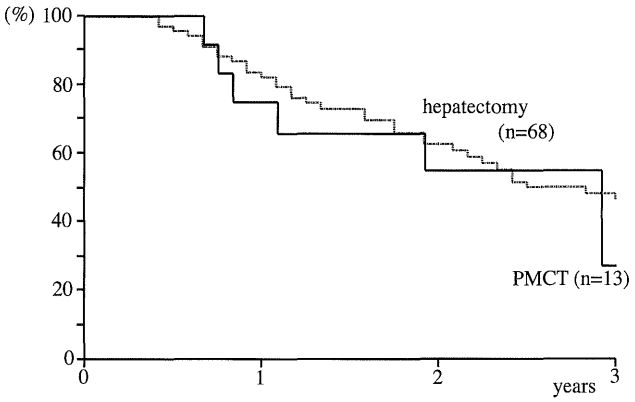

Fig. 2. Cumulative cancer free survival of patients who underwent PMCT or hepatectomy with a tumor of 3cm or less

Among the 13 patients in the PMCT group who had a maximum tumor diameter of 3cm or smaller, 6 had recurrence (single recurrence, 4; multiple recurrence, 2) (Table 3). Of the 4 patients with a single recurrence, 3 underwent PMCT again; the other patient (case 3), with tumor rupture, underwent transcatheter arterial embolization (TAE). Of the two patients with multiple recurrence, one (case 12) underwent TAE, while the other (case 13) who had serious liver failure, could not tolerate further treatment and died. Another patients (case 4) in whom liver failure developed 7 months after the second session of PMCT also died (Table 3).

Among the 6 patients in the PMCT group with a maximum tumor diameter of more than 3cm, the 5 with multiple tumors had recurrence (single recurrence, 2; multiple recurrence, 3) within a year. One (case 15) of the 2 patients with single recurrence underwent PMCT a second time, and the other (case 18) underwent surgery. The remaining 3 patients with multiple recurrence could not be treated further because of liver failure; 2 of these patients died (Table 4).

The survival rate was fairly good among patients with a maximum tumor diameter of 3cm or less: 100% at 1 year, 78.8% at 2 years, and 78.8% at 3 years in the PMCT group, and 97.1% at 1 year, 82.7% at 2 years, and 70.4% at 3 years in the hepatectomy group (Fig. 1). There was no significant difference between the two groups. The cancer-free survival rates were 75.0% at 1 year, 54.7% at 2 years, and 47.3% at 3 years in the PMCT group, and 87.3% at 1 year, 62.6% at 2 years, and 46.4% at 3 years in the hepatectomy group. No significant difference was found between the two groups (Fig. 2).

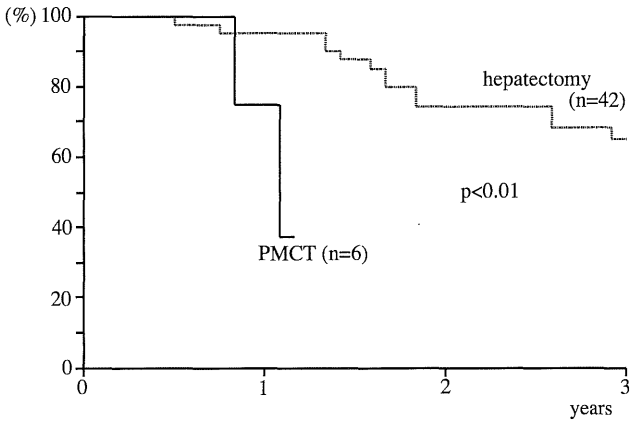

Fig. 3. Cumulative survival of patients who underwent PMCT or hepatectomy with a tumor of more than 3cm

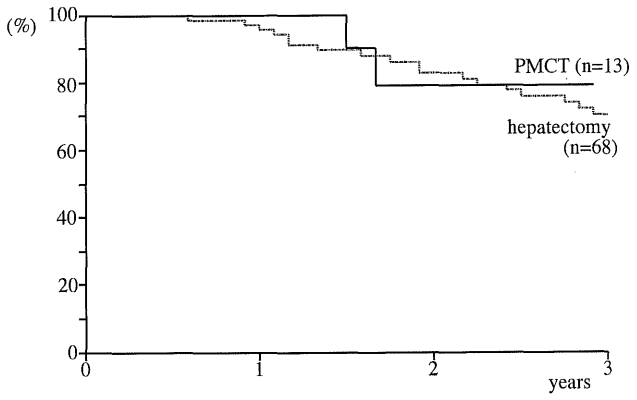

Fig. 4. Cumulative cancer free survival of patients who underwent PMCT or hepatectomy with a tumor of more than 3cm

Among patients with a maximum tumor diameter of greater than 3cm, the survival rate in the PMCT group (75.0% at 1 year and 37.5% at 13 months) was lower than that in the hepatectomy group (95.1% at 1 year, 74.2% at 2 years and 65.3% at 3 years) (Fig. 3). The cancer-free survival rate in the PMCT group (33.3% at 1 year) was lower than that in the hepatectomy group (78.1% at 1 year, 38.6% at 2 years and 27.3% at 3 years) (Fig. 4).

DISCUSSION

The hemostatic properties of microwave coagulation were investigated by Tabuse et al in 1979. They reported 3 beneficial effects of microwave coagulation: 1) complete control of bleeding or bile leakage; 2) the ability to seal veins up to 3mm in diameter, and 3) limited thermal damage caused by microwave energy, estimated to extend less than 10mm from the center of the coagulated tissue[3].

Although PMCT has been used not only to remove parenchymatous viscera[4] but also to treat liver cancer non-surgically[1,5], its efficacy has not yet been adequately evaluated. We therefore assessed the therapeutic usefulness of PMCT in the initial treatment of HCC as compared with hepatectomy. At baseline, patients in the PMCT group had severe liver cirrhosis on average. However, no liver failure occurred after treatment, indicating the high safety of PMCT.

In our hepatectomy cases of HCC, a significant difference of cumulative survival rate was seen between patients with a tumor of 3cm or less and those with a tumor of more than 3cm. Therefore, we divided patients into two groups: those with a tumor of 3cm or less and those with a tumor of more than 3cm.

The therapeutic usefulness of PMCT for liver tumors with a maximum diameter of greater than 3cm remains controversial. Comparing with surgery, it is difficult to accurately evaluate the effect of PMCT: 1) the number of the patients in PMCT groups were too small to evaluate the efficacy, 2) a high ratio of multiple tumors was seen in PMCT group compared with in hepatectomy group, 3) immediately after initial coagulation, the contour of the tumor becomes indistinct, and large tumors often do not undergo adequate coagulation after a single session of PMCT. The entire tumor may fail to coagulate after repeated PMCT. Insufficient coagulation can cause disseminated metastasis, and recurrence occurred in 5 of 6 patients whose tumors had a maximum diameter of more than 3cm at the time of initial treatment. In 3 of these patients, multiple metastases developed through the entire liver within a year. Another patient underwent surgery.

All 7 patients with multiple tumors had a recurrence within a year, and 5 had disseminated metastasis. Perhaps the multiple tumors were metastatic at the time of initial treatment. The possibility of multicentric tumorigenesis therefore merits further consideration.

In patients with single tumors of 3cm or less in diameter, however, PMCT was therapeutically equivalent to partial hepatectomy in terms of short-term outcome. Although long-term outcome has not yet been evaluated, available evidence suggests that PMCT may be an effective therapeutic option for HCC in patients with advanced underlying disease of the liver.

Seki et al[2] used PMCT to treat patients who had HCC with a maximum tumor diameter of 2cm or less. Disease recurred in only 3 of 18 patients, and the clinical outcome was as good as that with hepatectomy for up to 3 years after treatment.

On the basis of these results, we conclude that in the initial treatment of HCC, PMCT should be used to treat single tumors with a maximum diameter of 3cm or less; for tumors more than 3cm in diameter, surgical removal is recommended. PMCT is not indicated for multiple tumors, which have a high risk of metastasis. For multicentric tumors, further studies in increased numbers of

patients are required before firm recommendations can be made.

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