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● *Original Contribution*

ULTRASOUND-GUIDED PERCUTANEOUS MICROWAVE ABLATION TREATMENT OF INITIAL RECURRENT HEPATOCELLULAR CARCINOMA AFTER HEPATIC RESECTION: LONG-TERM OUTCOMES

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Abstract—This study aimed to evaluate the long-term outcomes after percutaneous microwave ablation (MWA) for patients with initial recurrent hepatocellular carcinoma (HCC) measuring ≤ 5 cm in diameter after hepatectomy. From May 2005 to December 2011, 89 patients with 116 initial recurrent HCCs after hepatectomy treated with percutaneous MWA were included in the study. One mo after MWA, the complete ablation rate was 91.0% (81/89). At 1, 3, 5 and 7 y, the respective overall and recurrence-free survival rates after percutaneous MWA were 73.3%, 53.7%, 39.6% and 17.3% and 58.5%, 26.4%, 22.0% and 11.0%. The cumulative incidence of local tumor progression (LTP) and the intra-hepatic distant recurrence (IDR)-free survival rates after MWA were 9.1%, 14.6%, 18.3% and 18.3% and 62.9%, 32.3%, 26.9% and 13.5% at 1, 3, 5 and 7 y, respectively. The multivariate analysis indicated that multiple tumors ($p = 0.006$), a poor Child-Pugh score ($p = 0.003$), serum α -fetoprotein (AFP) > 100 ng/mL ($p = 0.002$), and MWA treatment failure ($p = 0.000$) were risk factors that significantly affected overall survival, and MWA treatment failure ($p = 0.000$) was a risk factor that significantly affected IDR-free survival. In conclusion, percutaneous MWA is an effective therapeutic technique for initial recurrent HCC measuring ≤ 5 cm in diameter after hepatectomy. (E-mail: Liky20006@126.com) © 2015 World Federation for Ultrasound in Medicine & Biology.

Key Words: Ultrasound-guided, Percutaneous microwave ablation, Recurrent hepatocellular carcinoma, Survival rate.

Hepatocellular carcinoma (HCC) is the fifth most common type of cancer in the world (Bruix et al. 2005). The incidence of HCC recurrence in post-operative patients is high, and cumulative 5-y recurrence rates have been reported as 70%–100% (Forner et al. 2012; Wu et al. 2009). Repeat hepatectomy is a curative treatment and may prolong survival. However, it can only be performed in a small percentage of patients with recurrent HCC because of the small remnant liver volume, advanced tumor stage, or poor physical condition. The selection criteria are strictly controlled to improve patient outcome, and the rate of repeat resection has been reported to range from 10% to 31%

(Minagawa et al. 2003; Poon et al. 1999). Minimally invasive therapies have been developed in recent years, such as radiofrequency ablation (RFA) (Woo et al. 2013), microwave ablation (MWA) (Liu et al. 2013), percutaneous ethanol injection (PEI) (Ansari and Andersson 2012) and transarterial chemoembolization (TACE) (Peng et al. 2012), which have provided additional interventional approaches for patients.

Many reports have found that percutaneous RFA and MWA are effective and comparable to surgical resection for treating small HCC measuring ≤ 3 cm (Itoh et al. 2011; Liang et al. 2008). MWA is a potential therapeutic option for patients with liver tumors; local tumor control is possible for 94% of tumors measuring 3–5 cm (Liu et al. 2013). Currently, MWA is popular mainly in Eastern countries, such as China and Japan. To our knowledge, most studies have focused on evaluating the safety profile and efficacy of MWA, and only

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a few studies have reported the long-term outcomes; in these studies, the cumulative 3-y survival rate has been reported to be approximately 50% (Lu et al. 2005; Ohmoto et al. 2007). However, these few studies compared the therapeutic effect of percutaneous MWA versus RFA at treating HCC and included only a small number of patients in the MWA group. Furthermore, the 7-y survival rate after MWA has not been reported.

In this study, we aimed to evaluate the long-term outcomes after percutaneous MWA for patients with initial recurrent HCC measuring ≤ 5 cm in diameter after hepatectomy and to investigate the prognostic factors that affect overall survival and recurrence-free survival.

MATERIALS AND METHODS

Patient selection

From May 2005 to December 2011, 89 patients with 116 initial recurrent HCCs after hepatic resection underwent percutaneous MWA at the Hepatic Surgery Center, Tongji Hospital, and were enrolled in this retrospective study (83 male patients and 6 female patients; mean patient age, 49.7 ± 11.5 y; median patient age, 51.0 y; age range, 26.0–73.0 y). Hepatic resections, the first-line treatment modality for primary HCC, were performed in the same center from November 2002 to December 2010. This study was approved by our institutional human research review committee. Written informed consent was obtained from all of the patients before treatment. The patients who underwent percutaneous MWA included 68 (76.4%) with a single nodule and 21 (23.6%) with two to three nodules. Eighty-five patients were positive for hepatitis B surface antigen, and 4 were negative. Eighty-five patients (95.5%) were Child-Pugh class A, and four patients (4.5%) were Child-Pugh class B. The mean and median diameters of the primary HCC were 5.7 ± 2.9 cm and 5.0 cm (range, 1.1–15.0 cm), and the median number of tumors for hepatic resection was 1.0 (range, 1.0–2.0). The mean and median diameters of the recurrent HCC were 2.6 ± 1.0 cm and 2.6 cm (range, 0.8–5.0 cm), and the median number of tumors was 1.0 (range, 1.0–3.0) for percutaneous MWA. The clinicopathologic characteristics of all of the patients are summarized in Table 1.

The inclusion criteria were as follows: (i) Hepatectomy was defined as complete resection of all macroscopically detectable tumors and two or fewer tumor nodules, which were confirmed as hepatocellular carcinoma with liver cirrhosis by histopathologic examination; (ii) recurrent HCC < 5.0 cm in diameter and three or fewer tumor nodules; (iii) recurrent HCC suitable for percutaneous MWA under ultrasound guidance; patients with tumors close to the gastrointestinal or major branches of the intra-hepatic vasculature and bowels or with obstacles in the route to the tumor, such as lungs, ribs, or abundant

Table 1. Characteristics of the 89 patients with 116 recurrent HCCs

Clinicopathologic variables	Value
Gender	
Male versus female	83:6 (93.3%:6.7%)
Age (y)	
Mean \pm SD	$49.7 \pm 11.5^*$ (range, 26–73)
HBV	
Positive versus negative	85:4 (95.5%:4.5%)
Recurrent tumor size (cm)	
Mean \pm SD	$2.6 \pm 1.0^*$ (range, 0.8–5.0)
Type of recurrent HCC	
Early recurrence versus late recurrence	50:39 (56.2%:43.8%)
Recurrent tumor number	
Single versus multiple	68:21 (76.4%:23.6%)
Child-Pugh class	
A versus B	85:4 (95.5%:4.5%)
Serum AFP at ablation (ng/mL)	
< 100 versus ≥ 100	51:38 (57.3%:42.7%)

HCC = hepatocellular carcinoma; HBV = hepatitis B virus; AFP = α -fetoprotein.

* Mean \pm standard deviation.

ascites, were considered to be unsuitable for ablation; (iv) no extra-hepatic metastasis when MWA was performed; (v) no repeat hepatectomy or liver transplantation for second or additional recurrent HCCs during the follow-up period; and (vi) a prothrombin time ratio $> 50\%$ and a platelet count $\geq 50 \times 10^9/L$. The exclusion criteria were as follows: (i) more than three HCC nodules at the time of MWA treatment ($n = 1$); (ii) recurrent HCC > 5 cm ($n = 13$); (iii) extra-hepatic metastasis before MWA treatment ($n = 2$); and (iv) patients with second or additional recurrent HCCs who were treated with repeat hepatectomy during the follow-up period ($n = 9$).

HCC diagnosis

Recurrent HCC with liver cirrhosis was diagnosed based on the non-invasive criteria proposed by the American Association for the Study of Liver Disease Practice Guideline (Bruix et al. 2005). Nodules found by ultrasound (US), computed tomography (CT) or magnetic resonance imaging (MRI) exhibited the typical features of HCC (arterial hypervascularity and venous or delayed phase washout) by two different contrast-enhanced imaging techniques, such as contrast-enhanced MRI (CEMRI) (1.5-T, Signa HDxt, GE Healthcare, Pittsburgh, PA, USA), contrast-enhanced CT (CECT) (Bright-Speed 16; Light-Speed Volume CT, GE Healthcare, Pittsburgh, PA, USA), or contrast-enhanced ultrasound (CEUS) (IU22, Philips, Andover, MA, USA; LOGIQ E9 or LOGIQ 9, GE Healthcare, Pittsburgh, PA, USA) ($n = 88$). A liver biopsy was performed in one patient who did not meet the non-invasive diagnostic criteria. When recurrences were diagnosed, the patients were treated with percutaneous MWA. For CEUS examination, a

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