Ann Surg Oncol (2011) 18:3650–3656
DOI 10.1245/s10434-011-1831-z

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – HEPATOBILIARY TUMORS

Efficacy of Surgical Microwave Therapy in Patients with Unresectable Hepatocellular Carcinoma

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ABSTRACT

Background. We aimed to evaluate the efficacy and long-term outcome in surgical microwave therapy (MW) for patients with unresectable hepatocellular carcinoma (HCC).

Methods. An institutional review board approved and single-institutional study of surgical MW of unresectable HCC was conducted from May 2003 to December 2010. The median follow-up period was 19 months (range 1–77 months).

Results. A total of 60 patients underwent 143 surgical MW for unresectable HCC. Of these, 15 patients had initial HCC and 45 had recurrent HCC. The median tumor size of HCC was 1.95 cm (range 0.8–3.3 cm). The median numbers of nodules that underwent surgical MW were 2 (range 1–9). Multinodular type was found in 33 patients (55%). Morbidity was 18.3%, and there was zero mortality. Also, 3 patients (5%) had incomplete MW. Of the 60 patients, 39 (65%) had recurrence, and 7 (11.6%) had local recurrence. The 1- and 3-year recurrence-free survival rates of the patients who underwent surgical MW for initial HCC were 55.1 and 36.7%, respectively, and those for recurrent HCC were 41.6% and 8.8%, respectively. A tumor size $\geq$ 2.0 cm and multiple nodules were selected as independent and significant indicators for recurrence of the disease. The 1-, 3-, and 5-year overall survival rates after the surgical MW procedure were 93.9, 53.8, and 43.1%, respectively. A level of des-gamma carboxyprothrombin (DCP) was an independent and significant indicator for overall survival.

Conclusions. Surgical MW is an effective method for treating initial or recurrent unresectable HCC, and it can be undergone safely.

Hepatocellular carcinoma (HCC) is one of the most common cancers worldwide and generally occurs in a cirrhotic liver.[1] In most cases, hepatic resection is the best curative treatment for HCC.[2–4] However, there are some factors that limit the use of surgical resection. Local ablation therapies (ethanol injection therapy [EIT], microwave therapy [MW], and radiofrequency ablation [RFA]) have emerged to be safe and effective treatment of small HCC.[5,6]

MW has been used clinically in Japan for several years.[7–9] MW refers to the use of electromagnetic methods for inducing tumor destruction using devices with frequency $\geq$ 900 MHz.[9,10] The rotation of the dipole molecules accounts for the efficient amount of heat generated during microwave coagulation.[11] One or more molecules are dipoles with unequal electrical charge distribution, and they attempt to reorient continuously at the same rate in the microwave's oscillating electric field. As a result of the microwave transmission, the water molecules flip back and forth at a billion times a second leading to this vigorous movement to produce friction and heat, which leads to cellular death via coagulation necrosis.

With the advent of MW, we began to perform surgical approach MW in patients with HCC that cannot be resected and cannot be accurately accessed by a percutaneous approach. Here we present the results of performing surgical approach MW in patients with unresectable HCC. We evaluate the validity and identify the prognostic factors of surgical approach MW.

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First Received: 10 March 2011;
Published Online: 15 June 2011

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METHODS

Patients

An institutional review board approved and single-institutional study of surgical MW of unresectable HCC was conducted from May 2003 to December 2010. A total of 60 patients (43 male, 17 female; age range 47–83 years; mean age 67.7 years) underwent 143 surgical MW for HCC at the Department of Surgery, Fukuoka City Hospital. Of these patients, 15 had initial HCC and 45 had recurrent HCC. The median follow-up period was 19 months, range 1–77 months. The segmental locations of the 143 lesions included 3 HCCs located in segment 1, 8 in segment 2, 13 in segment 3, 17 in segment 4, 13 in segment 5, 23 in segment 6, 20 in segment 7, and 46 in segment 8, as defined by Couinaud.

All patients underwent a thorough examination including laboratory tests to evaluate liver function, tumor marker such as alpha-fetoprotein (AFP) and des-gamma carboxyprothrombin (DCP), radiological assessment of tumor location by ultrasonography, contrast-enhanced computed tomography (CT), magnetic resonance imaging, mesenteric arteriography, and computed tomographic portography. All of the patients were evaluated at a multidisciplinary tumor board conference of surgical oncologists, medical oncologists, and interventional radiologists. For patients with disease that was believed to be unresectable because of the number, distribution, and/or location of the tumors, or because of patient comorbid factors including advanced age or refusal to undergo the hepatic resection, surgical MW was considered. Patients with unresectable tumors located in a position amenable to percutaneous RFA or MW were treated by this approach. Surgical approach was offered in the following circumstances; tumor morphology required multiple ablation therapies; tumors located near the dome of the liver, for which percutaneous ablation might cause pneumothorax or damage to the diaphragm; or tumors located near the visceral organs such as the gallbladder, colon, or stomach. A thoracotomy with a short skin incision was selected if tumor located near the dome of the liver. In select patients who had not undergone a previous upper abdominal operation, a laparoscopic approach was considered if tumor position was favorable. However, only 2 patients were treated by the laparoscopic approach.

All patients underwent surgical MW. The location and size of the HCC nodules had been confirmed with the ultrasound probe (Aloka Inc., Tokyo, Japan). The microwave was generated by a magnetron in a 2450 MHz microwave generator (Microtaze OT-110 M, HS-15 M; Azwell Co., Osaka, Japan). Microwave irradiation was administered for 60 s at a power setting of 65 W per pulse using a microwave electrode 1.6 mm in diameter and 25 cm in length.[8,12,13] Microwave irradiation was applied initially from the ventral caudal site to the dorsal cephalad site across the entire tumor, including the area larger than 5 mm outside the tumor margin. Postoperative complications were defined as any event that required specific medical or surgical treatment. The ultimate efficacy of MW was assessed using contrast-enhanced CT, 1–2 weeks after procedure when the patient was still in our hospital and within 1–2 months after discharge; hypoattenuating non-enhancing areas on both early- and late-phase images with at least 5 mm wider than the actual target lesion size were regarded as representing complete necrosis. Mortality was defined as in-hospital death or death within 30 days after surgery. The patients were strictly followed up after surgical MW. A monthly measurement of AFP and DCP and monthly bedside ultrasonography were performed. Contrast-enhanced CT was performed every 3 months by radiologists. An angiographic examination was done after admission when there was a strong suspicion of disease recurrence.

Statistical Analysis The cutoff values of clinical variables were determined as described previously.[14] Continuous variables were compared using the Mann–Whitney *U* test. Categorical variables were compared using a χ^2 test or Fisher exact test. The overall survival and disease-free survival rates were calculated using the product limit method of Kaplan–Meier method and compared using the log-rank test. The Cox proportional hazards model was used in multivariate analysis of survival data. Differences were considered significant at $P < 0.05$. All statistical analyses were performed using the StatView 5.0 (Abacus Concepts, Berkeley, CA).

RESULTS

Perioperative patient characteristics are described in Table 1. Of these patients, based on Child-Pugh classification, 41 (68.3%) were considered class A, 19 patients (31.7%) class B, and none of the patients were class C. The maximal diameter of HCC for all patients ranged from 0.8 to 3.3 cm (median 1.95 cm). The median numbers of nodules that underwent surgical MW were 2 and a range of 1–9. Also, 1–5 MW sessions per nodule were performed (median 2 sessions). A total of 33 patients (55%) had multinodular type. Of 60 patients, 11 (18.3%) sustained postoperative complications. Postoperative complications included pleural effusion ($n = 4$), ascites ($n = 4$), bile leakage ($n = 3$), wound infection ($n = 2$), intra-abdominal abscess ($n = 1$), and intra-abdominal bleeding ($n = 1$). There were no perioperative deaths. Although the numbers

TABLE 1 Characteristics on 60 patients who underwent surgical microwave therapy (MW)

Variables	Value
Mean age, years	67.7 (range 47–83)
Men/women	43/17
Initial/recurrent HCC	15/45
Background liver disease	
Hepatitis B virus (HBV)	8
Hepatitis C virus (HCV)	47
HBV + HCV	1
No infection	4
Child-Pugh classification (A/B/C)	41/19/0
ASA score (2/3)	27/33
Median AFP (ng/ml)	19.6 (range 1.7–1205)
Median DCP (mAU/ml)	31 (range 7.2–5662)
Median tumor size (cm)	1.95 (range 0.8–3.3)
Median number of tumor	2 (range 1–9)
Solitary/multinodular tumor	27/33
Laparotomy/thoracotomy	23/37
Median duration of surgery (min)	100 (range 48–415)
Postoperative complication	11 (18.3%)
Mortality	0 (0%)
Complete effectiveness of MW	57 (95.0%)
Total recurrence patients	39 (65.0%)
Local recurrence	7 (11.6%)
Intrahepatic distant recurrence	32 (53.4%)

HCC hepatocellular carcinoma, *ASA* American Society of Anesthesiologists, *AFP* alfa fetoprotein, *DCP* des-gamma carboxyprothrombin

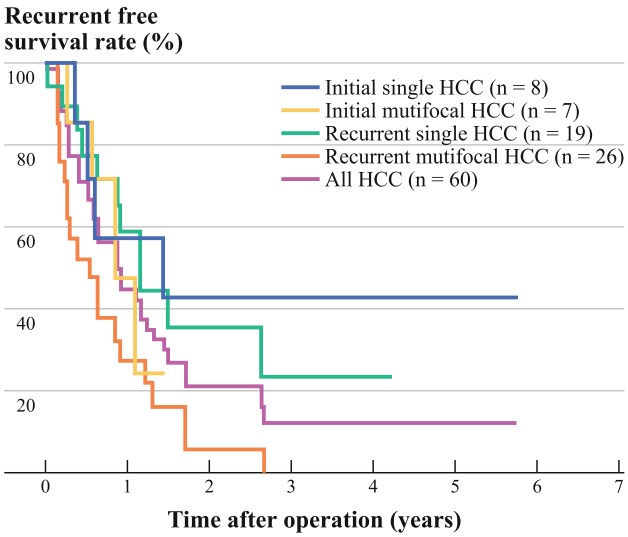


FIG. 1 Recurrence-free survival curve of patients with surgical microwave therapy for unresectable HCC

and length of the irradiation treatments varied, in 57 of the 60 patients (95%) treatment with surgical MW was judged to have been complete, on contrast-enhanced CT carried out 1–2 weeks after procedure when the patient was still in our hospital and within 1–2 months after discharge. Of the remaining patients, 3 had to have hepatic arterial therapy.

There were recurrences of HCC nodules in 39 of the 60 patients (65%) underwent surgical MW. The remaining 21 patients (35%) have had no recurrence with a longest observation period of 70 months. There were 7 patients (11.6%) in this study who experienced local recurrence, which was considered to derive from the same or adjacent place of the tumor underwent surgical MW, at 3–11 months (median 7 months). In the other 32 patients (53.4%) there was intrahepatic distant recurrence at 1–32 months (median 8 months). Of these patients, 3 had initial HCC and 4 had recurrent HCC. The segmental locations of 7 locally recurrent lesions included 1 HCC located in segment 6, and 6 in segment 8, as defined by Couinaud. All local recurrences were found within the dorsal part of the areas treated with surgical MW. Of the 7 patients, 6 underwent thoracotomy MW, but there were statistical difference between laparotomy and thoracotomy MW about local recurrence. The median diameter of nodules that underwent surgical MW in patients with local recurrence after the treatment were 2.5 cm (range 1.5–3.0 cm), which was significantly larger than that in patients without local recurrence after the treatment (median 1.9 cm, range from 0.8 to 3.3 cm, $P = 0.0226$). When the recurrence-free survival rate for all 60 patients with surgical MW was analyzed using the Kaplan–Meier method, the 1-, 3-, and 5-year recurrence-free survival rates were 45.0, 21.4, and 12.9%, respectively (Fig. 1). The recurrence-free survival rates in initial and recurrent solitary HCCs were significantly better than that in recurrent multifocal HCC ($P = 0.0413$ and .0186, respectively). In a univariate analysis of recurrence-free survival, significant differences were observed in the following 2 variables; tumor size ≥ 2.0 cm ($P = 0.0108$) and multiple nodules ($P = 0.0121$) (Table 2). A level of DCP > 300 mAU/ml showed a tendency to poorer recurrence-free survival ($P = 0.0659$). The results of multivariate analysis are shown in Table 3. A tumor size ≥ 2.0 cm ($P = 0.0316$) and multiple nodules ($P = 0.0342$) were selected as independent and significant indicators for recurrence-free survival.

Figure 2 exhibits the overall survival for all patients after surgical MW. The 1-, 3-, and 5-year overall survival rates were 93.9, 53.8, and 43.1%, respectively. There was no significant differences in overall survival rates between each group including initial solitary HCC, initial multifocal HCC, recurrent solitary, and recurrent multifocal HCC. Table 4 shows the results of a univariate analysis used to identify the significant factors closely related to the overall survival rate after surgical MW in patients with

TABLE 2 Variables of patients with hepatocellular carcinoma (HCC) treated with surgical microwave therapy (MW) regarding recurrence-free survival rate

Variables	1-year survival (%)	3-year survival (%)	5-year survival (%)	*P* value
Age (years)				
0: < 70 ($n = 32$)	43.9	0	0	0.1337
1: ≥ 70 ($n = 28$)	46.8	31.2	31.2	
Sex (male/female)				
0: male ($n = 43$)	44.6	5.5	–	0.4220
1: female ($n = 17$)	44.4	33.3	33.3	
HCC				
0: initial ($n = 15$)	55.1	36.7	36.7	0.2268
1: recurrent ($n = 45$)	41.6	8.8	–	
ASA				
0: grade II ($n = 27$)	51.1	15.1	–	0.7888
1: grade III ($n = 33$)	41.1	10.4	10.4	
Hepatitis B virus				
0: absent ($n = 51$)	47.2	15.6	15.6	0.2922
1: present ($n = 9$)	37.5	0	0	
Hepatitis C virus				
0: absent ($n = 12$)	40.0	0	0	0.6172
1: present ($n = 48$)	47.0	14.2	14.2	
Diabetes mellitus				
0: absent ($n = 34$)	43.0	18.8	–	0.7664
1: present ($n = 26$)	46.9	11.9	11.9	
Hypertension				
0: absent ($n = 43$)	45.0	7.4	–	0.5420
1: present ($n = 17$)	41.7	16.7	16.7	
AST (IU/l)				
0: < 70 ($n = 46$)	43.9	14.1	14.1	0.3607
1: ≥ 70 ($n = 14$)	50.0	13.3	_	
AST (IU/l)				
0: < 70 ($n = 47$)	44.8	13.6	13.6	0.9584
1: ≥ 70 ($n = 13$)	45.5	11.4	–	
Albumin (g/dl)				
0: > 3.4 ($n = 32$)	60.0	16.4	16.4	0.3607
1: ≤ 3.4 ($n = 28$)	28.1	9.4	–	
Total bilirubin (mg/dl)				
0: < 1.0 ($n = 30$)	50.0	24.3	24.3	0.2738
1: ≥ 1.0 ($n = 30$)	40.7	6.3	–	
Platelets ($\times 10^4$/mm^3)				
0: > 10 ($n = 23$)	55.7	17.4	17.4	0.3068
1: ≤ 10 ($n = 37$)	38.6	9.2	–	
Child-Pugh class				
0: grade A ($n = 41$)	51.9	19.1	19.1	0.2644
1: grade B ($n = 19$)	31.8	–	–	
AFP (ng/ml)				
0: < 200 ($n = 52$)	48.2	12.4	12.4	0.8865
1: ≥ 200 ($n = 8$)	28.6	–	–	
DCP (mAU/ml)				
0: ≤ 300 ($n = 51$)	51.6	15.8	15.8	0.0659
1: > 300 ($n = 9$)	12.5	0	0	
Tumor size (cm)				
0: < 2.0 ($n = 30$)	62.7	22.1	22.1	0.0108
1: ≥ 2.0 ($n = 30$)	26.5	0	0	
Tumor nodule				
0: solitary ($n = 27$)	58.3	28.4	28.4	0.0121
1: multiple ($n = 33$)	32.5	0	0	
Milan criteria				
0: met ($n = 45$)	47.2	18.1	18.1	0. 3287
1: not met ($n = 15$)	35.0	0	0	
Groups of HCC				
Initial solitary ($n = 8$)	57.1	42.9	42.9	–
Initial multifocal ($n = 7$)	47.6	–	–	
Recurrent solitary ($n = 19$)	58.6	23.4	23.4	
Recurrent multifocal ($n = 26$)	27.2	0	0	
Postoperative complication				
0: absent ($n = 49$)	45.7	14.0	14.0	0.4413
1: present ($n = 11$)	40.4	10.1	–	

ASA American Society of Anesthesiologists, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *AFP* alfa fetoprotein, *DCP* des-gamma carboxyprothrombin

TABLE 3 The results of a multivariate analysis using the Cox proportional hazards model in patients with hepatocellular carcinoma who underwent surgical microwave therapy (MW) regarding recurrence-free survival rate

Variables	Hazard ratio	95% CI	*P* value
Multiple nodules	2.049	1.054–3.984	0.0342
Tumor size ≥ 2.0 cm	2.092	1.067–4.098	0.0316

95% CI 95% confidence interval

unresectable HCC. The poor prognostic factors were found to include Child-Pugh classification grade B ($P = 0.0399$), a serum level of albumin ≤ 3.4 mg/dl ($P = 0.0455$), a level of AFP ≥ 200 ng/ml ($P = 0.0365$) and a level of DCP > 300 mAU/ml ($P < 0.0001$). The Cox proportional hazards model was used to assess the effect of different variables on overall survival. Multivariate analysis identified poor prognostic factor including a level of DCP > 300 mAU/ml ($P = 0.0018$) as influencing overall survival rate after surgical MW in patients with HCC.

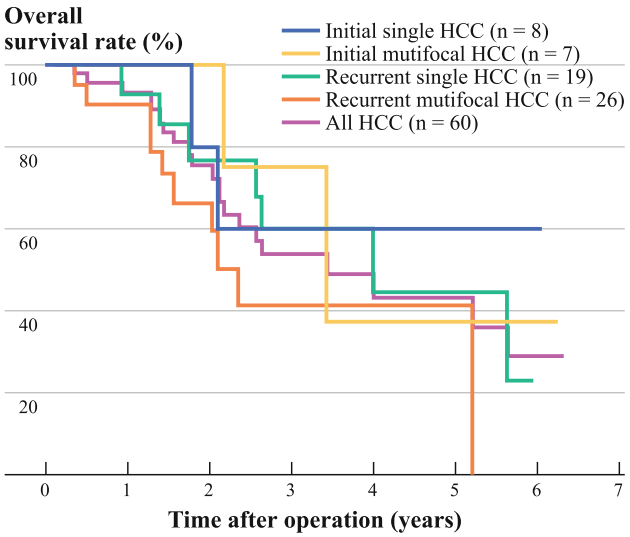


FIG. 2 Overall survival curve of patients with surgical microwave therapy for unresectable HCC

DISCUSSION

MW has been reported to be effectively delivered through open laparotomy, laparoscopically, percutaneously, and even thoracoscopically in the appropriate patients.[9,15,16] Surgical MW has advantages over the percutaneous procedure. Tumors near stomach, colon, kidney, or diaphragm can be treated with surgical MW. Intraoperative ultrasonography examination can identify very small hepatic nodules that may be not detectable on preoperative imaging.[17,18] The limitation of surgical approach is that these require general anesthesia and intra-abdominal access, which has the potential to be a greater risk for patients with marginal hepatic function.

Only a few series of surgical MW of HCC have been reported. Seki et al. performed laparoscopic microwave coagulation therapy for patients with HCCs that were located near the liver surface and were unable to be treated with percutaneous locoregional therapies.[15] The 1-, 3-, and 5-year overall survival rates in patients with laparoscopic microwave coagulation therapy were 97, 81, and 43%, respectively. In the study of Martin et al., 100 patients who had hepatic malignancies underwent surgical microwave ablation.[19] The cumulative survival rate for patients with HCC at 3 years was about 50%. In our report, the 1-, 3-, and 5-year overall survival rates of 60 patients treated with surgical MW for 143 unresectable HCCs were 93.9, 53.8, and 43.1%, respectively. Base on these data, we believe that surgical MW is a useful therapeutic option for patients with unresectable HCC.

When the recurrence was assessed, with respect to local recurrence, it was reported to occur in approximately 10%

TABLE 4 Variables of patients with hepatocellular carcinoma (HCC) treated with surgical microwave therapy (MW) regarding overall survival rate

Variables	1-Year survival (%)	3-Year survival (%)	5-Year survival (%)	*P* value
Age (years)				
0: < 70 ($n = 32$)	96.8	54.4	35.0	0.7728
1: ≥ 70 ($n = 28$)	90.9	53.6	53.6	
Sex (male/female)				
0: male ($n = 43$)	94.7	53.5	46.8	0.6802
1: female ($n = 17$)	91.7	57.0	38.0	
HCC				
0: initial ($n = 15$)	100	66.7	50.0	0.1682
1: recurrent ($n = 45$)	91.7	49.3	39.4	
ASA				
0: grade II ($n = 27$)	100	53.8	29.9	0.7012
1: grade III ($n = 33$)	89.5	54.3	54.3	
Hepatitis B virus				
0: absent ($n = 51$)	95.6	55.4	48.5	0.2067
1: present ($n = 9$)	83.3	41.7	0	
Hepatitis C virus				
0: absent ($n = 12$)	78.7	47.3	0	0.2144
1: present ($n = 48$)	97.7	55.8	48.8	
Diabetes mellitus				
0: absent ($n = 34$)	92.1	39.7	21.2	0.0821
1: present ($n = 26$)	96.0	68.1	68.1	
Hypertension				
0: absent ($n = 43$)	91.6	46.0	34.5	0.2347
1: present ($n = 17$)	100	70.7	56.6	
AST (IU/l)				
0: < 70 ($n = 46$)	92.0	55.1	46.0	0.8511
1: ≥ 70 ($n = 14$)	100	51.1	38.4	
AST (IU/l)				
0: < 70 ($n = 47$)	92.3	50.4	42.0	0.5889
1: ≥ 70 ($n = 13$)	100	63.5	50.8	
Albumin (g/dl)				
0: > 3.4 ($n = 32$)	95.8	69.8	58.2	0.0455
1: ≤ 3.4 ($n = 28$)	91.8	39.1	29.3	
Total bilirubin (mg/dl)				
0: < 1.0 ($n = 30$)	95.2	49.4	49.4	0.5442
1: ≥ 1.0 ($n = 30$)	92.6	56.9	39.8	
Platelets ($\times 10^4/mm^3$)				
0: > 10 ($n = 23$)	95.2	54.4	46.6	0.6752
1: ≤ 10 ($n = 37$)	93.2	53.5	40.1	
Child-Pugh class				
0: grade A ($n = 41$)	96.7	62.7	48.3	0.0399
1: grade B ($n = 19$)	88.9	37.0	37.0	
AFP (ng/ml)				
0: < 200 ($n = 52$)	95.6	61.4	49.3	0.0365
1: ≥ 200 ($n = 8$)	85.7	17.9	–	

TABLE 4 continued

Variables	1-Year survival (%)	3-Year survival (%)	5-Year survival (%)	*P* value
DCP (mAU/ml)				
0: ≤ 300 ($n = 51$)	95.6	67.5	54.1	<0.0001
1: > 300 ($n = 9$)	85.7	0	0	
Tumor size (cm)				
0: < 2.0 ($n = 30$)	96.4	74.3	61.9	0.0636
1: ≥ 2.0 ($n = 30$)	91.6	34.0	22.7	
Tumor nodule				
0: solitary ($n = 27$)	95.0	58.7	48.9	0.2305
1: multiple ($n = 33$)	92.8	49.4	37.0	
Milan criteria				
0: met ($n = 45$)	92.2	53.3	41.1	0.6550
1: not met ($n = 15$)	100	56.3	56.3	
Groups of HCC				
Initial solitary ($n = 8$)	100	60.0	60.0	–
Initial multifocal ($n = 7$)	100	75.0	37.5	
Recurrent solitary ($n = 19$)	92.9	59.6	44.7	
Recurrent multifocal ($n = 26$)	90.4	41.5	41.5	
Postoperative complication				
0: absent ($n = 49$)	97.2	56.6	43.7	0.4344
1: present ($n = 11$)	80.0	42.9	42.9	

ASA American Society of Anesthesiologists, *AST* aspartate aminotrasferase, *ALT* alanine aminotrasferase, *AFP* alfa fetoprotein, *DCP* des-gamma carboxyprothrombin

of cases.[15,20] The current study data indicated that the incidence of local recurrence was 11.6%. There was a significant difference in the median diameter of nodules that underwent surgical MW between patients with and without local recurrence. Of 7 patients with local recurrence after surgical MW, 6 (85.7%) had nodules ≥ 2 cm in diameter. Moreover, multivariate analysis identified unfavorable factors including a tumor size ≥ 2.0 cm as influencing recurrence-free survival after surgical MW in patients with unresectable HCC. These results suggest that we need to develop a better technique for patients with unresectable HCCs ≥ 2 cm in diameter.

Patients with a level of DCP > 300 mAU/ml had poor overall survival after surgical MW by multivariate analysis. However, a preoperative DCP level of > 300 mAU/ml was not correlated with tumor size and a number of nodules in this study (data not shown). Multiple nodules were selected as one of independent and significant indicators for recurrence of the disease in multivariate analysis, but did not indicate poor overall survival by univariate analysis. DCP has been well established as a sensitive and specific tumor marker in patients with HCC and has been correlated with the development of portal venous invasion.[21–23] These findings suggest that higher DCP with HCC revealed the existence of portal venous invasion that could not be treated by surgical MW. On the other hand, patients with multiple nodules and a lower level of DCP are thought to have multicentric occurrence of HCCs.[24] Surgical MW might be a good indication for patients with unresectable multinodular HCCs derived from multicentric occurrence and a lower level of DCP.

Liver transplantation has become a widely accepted therapy for patients with HCC carrying a single tumor ≤ 5 cm or multiple ≤ 3 nodules ≤ 3 cm in size.[25] In this study, 45 patients were within the Milan criteria, whereas 15 were not. The 1-, 3-, and 5-year overall survival rates after the surgical MW procedure of the patients who fulfilled the Milan criteria were 92.2, 53.3, and 41.1%, respectively, whereas those for the patients who exceeded the criteria were 100, 56.3, and 56.3%, respectively ($P = 0.6550$, Table 4). In the study of Taketomi et al., 90 patients underwent living donor liver transplantation (LDLT).[22] The 1- and 3-year overall survival rates of the patients who underwent LDLT for HCC within the Milan criteria were 100 and 83.3%, respectively, whereas those for the patients who exceeded the criteria were 86.4 and 70.0%, respectively. Together with this study, we think that liver transplantation might be a more adequate management for patients with HCC within the Milan criteria, but controversial for patients with HCC that exceeds the Milan criteria. Recently, sorafenib is an oral multikinase inhibitor and improves overall survival in patients with advanced HCC.[26] However, most patients who responded to sorafenib had stable disease, and a complete response is rare. Further investigation of a great number of patients is needed.

The first limitation of this study is its single institutional review. The second is a lack of statistical power given their small sample sizes. These limitations will need to be verified with multi-institutional reviews and possible clinical studies.

In conclusion, the 1-, 3-, and 5-year overall survival rates after surgical MW for unresectable HCC were 93.9, 53.8, and 43.1%, and the 1-, 3-, and 5-year recurrence-free survival rates were 45.0, 21.4, and 12.9%, respectively. Surgical MW was considered to be safe and effective for unresectable HCC. A tumor size ≥ 2.0 cm and multiple nodules were significant independent factors for recurrence of the disease.

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