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# Comparative Study of Application of Computed Tomography/Ultrasound and Computed Tomography Imaging Guidance Methods in the Microwave Ablation of Liver Cancer

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**Purpose:** The aim of the study is to assess the clinical value of the combined computed tomography (CT)/ultrasound (US) guidance in microwave ablation (MWA) for hepatocellular carcinoma (HCC).

**Methods:** From July 16, 2016, to June 20, 2021, medical records of 150 HCC patients treated with MWA were retrospectively analyzed. Ninety-two patients with 115 liver tumors underwent MWA under combined CT/US guidance, and 58 patients with 73 liver tumors received MWA under CT guidance alone. The clinical efficacy of combined CT/US-guided MWA was analyzed. We compared the complications, procedure time, and CT scan times between the 2 groups.

**Results:** The total complete ablation rate and complete ablation rate of high-risk location tumors were significantly higher in the group treated with combined CT/US guidance ( $P = 0.0471$  and  $P = 0.0347$ , respectively), the imaging guidance modality (odds ratio, 0.303; 95% confidence interval [CI], 0.095–0.970;  $P = 0.044$ ) was an independent factor for ablation efficacy. These 2 groups also had significant differences in the procedure time ( $P = 0.0171$ ), the incidence rate of pneumothorax ( $P = 0.0209$ ), abdominal pain ( $P = 0.0196$ ), nausea or vomiting ( $P = 0.0026$ ), and intraoperative CT scan times ( $P < 0.001$ ). The overall complication rates ( $P = 0.4023$ ) and recurrence rates ( $P = 0.5063$ ) between the 2 groups were not statistically significant. However, CT/US group has a better short-term progressive free survival (log-rank  $P = 0.103$ , Breslow  $P = 0.030$ ). In multivariate analysis, guidance modality (hazard ratio, 0.586; 95% CI, 0.368–0.934;  $P = 0.025$ ) and Barcelona Clinic Liver Cancer stage (hazard ratio, 2.933; 95% CI, 1.678–5.127;  $P < 0.001$ ) were risk factor for progressive free survival.

**Conclusions:** Percutaneous MWA under the combined CT/US guidance for HCC can improve clinical benefits.

**Key Words:** hepatocellular carcinoma, comparison, microwave ablation, computed tomography, ultrasound

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Liver cancer is the second most common cause of cancer deaths worldwide.<sup>1</sup> The main pathological type of primary liver cancer is hepatocellular carcinoma (HCC, 85%–90%). The standard treatment methods for liver cancer are surgery, liver transplantation,

immunity therapy, and local minimally invasive treatment. Local ablation therapy is an essential part of the minimally invasive treatment of liver cancer. Ablation therapy has been extensively developed in recent years and can alternate surgery or liver transplantation.<sup>2</sup> Thermal ablation is the most common form of percutaneous ablation. According to the description of thermal ablation therapy in the latest updates guidelines, there is no significant difference between local ablation and surgical resection. Both methods can obtain a radical cure for early-stage liver cancer.<sup>3–8</sup> These guidelines are applicable for patients with a single lesion (diameter  $\leq 5$  cm); patients with 2 to 3 lesions (maximum lesion diameter  $\leq 3$  cm); patients with no invasion of blood vessels, bile duct, and adjacent organs; distant metastasis; and Barcelona Clinic Liver Cancer (BCLC) stage 0-A. For this reason, lately, many patients who cannot or are unwilling to undergo surgery have chosen to opt for thermal ablation to reduce the risk of tumor progression.

The commonly used thermal ablation treatment methods mainly include microwave ablation (MWA) and radiofrequency ablation (RFA). Both RFA and MWA rely on intraoperative imaging guidance techniques, such as computed tomography (CT), ultrasound (US), and magnetic resonance imaging (MRI). These imaging guidance techniques have advantages and disadvantages. There are many clinical applications of MWA under the guidance of single imaging. Microwave ablation under CT guidance has become increasingly common in recent years; this imaging guidance is not affected by gas and bone, especially for top-of-diaphragm lesions. Computed tomography-guided percutaneous radiofrequency ablation is usually used in cases where US guidance is difficult.<sup>9,10</sup> Previous studies have also demonstrated that liver tumors could not be detected using the US in approximately 15% and 20% of the cases.<sup>11,12</sup> However, it has certain limitations, such as no real-time capability, long operation time, and intraoperative radiation exposure. Puncturing under CT guidance is also influenced by patients' respiratory movements. The advantages of US-guided ablation are convenience, real-time capability, lower cost, and no intraoperative radiation. It has some limitations, such as vaporization of the lesion during

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The authors declare no conflict of interest.

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All authors consent to the publication of this manuscript.

The institutional review board of our hospital approved this retrospective study using existing patient data and images from the Yanbian University Hospital.

The data sets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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**TABLE 1.** Characteristics of HCC Patients in the Combined CT/US-Guided Group and CT Guided Group

Demographics and Characteristics (N = 150)	Total	CT (n = 58)	CT/US (n = 92)	P
Sex				
Male	109	42	67	0.9560
Female	41	16	25	
BCLC stage				
O	58	25	33	0.3756
A	92	33	59	
High-risk location tumor	133	53	80	0.6555
Tumor number, mean ± SD (range)	1.25 ± 0.50 (1–3)	1.26 ± 0.48 (1–3)	1.25 ± 0.52 (1–3)	0.690
Tumor size, mean ± SD (range), cm	1.92 ± 0.92 (0.5–5.0)	1.76 ± 0.74 (0.5–4.6)	2.02 ± 1.02 (0.7–5.0)	0.252
Microwave ablation session, mean ± SD (range), time	1.09 ± 0.29 (1–2)	1.16 ± 0.36 (1–2)	1.05 ± 0.23 (1–2)	0.042

ablation, which may interfere with the operator's field of view, resulting in a smaller or over ablation range. Moreover, US guidance is also affected by gas and bone. It is determined that the advantages and disadvantages of the 2 guidance methods can complement each other if CT and US are combined. The resulting guidance mode for MWA would have both real-time ablation and a higher detection rate of lesions.

Several previous studies evaluated the outcomes of single imaging guidance for percutaneous MWA of HCC. However, the studies on the efficacy of CT/US combined guidance in percutaneous HCC MWA are still limited. It is essential to determine whether the combined CT/US-guided MWA can result in better clinical benefit than the CT-guided MWA alone. The objective of this study was to fill this gap in knowledge by estimating the progression-free survival (PFS), complete ablation rate, high-risk location CAR, recurrence rate, complications, intraoperative CT scan times, MWA session, and procedure time between 2 groups.

## MATERIAL AND METHODS

### Study Design and Patient Selection

All patients involved in this study were from the same hospital. Data were collected from 150 patients with 188 liver tumors between January 16, 2016, and June 20, 2021 (Table 1). Ninety-two patients with 115 liver tumors underwent combined US/CT-guided percutaneous MWA, and 58 patients with 73 liver tumors received percutaneous MWA under CT guidance alone. The inclusion criteria of the patients were as follows: (1) patients with BCLC 0-A stage; (2) patients who refused or were unable to undergo liver resection or liver transplantation; (3) tumor was pathologically confirmed diagnosis of HCC; (4) patients for whom the diameter of a single tumor is less than 5 cm; (5) patients for whom the diameter of up to 3 tumors is less than 3 cm; (6) without severe heart disease or pulmonary disease; (7) no extrahepatic metastases and no tumor invasion of blood vessels or bile ducts; (8) blood platelet count greater than  $50 \times 10^9/L$ ; and (9) patients with normal prothrombin time, activated partial thromboplastin time, and more than 50% fibrinogen activity. A tumor in a high-risk location is defined if the distance between the tumor margin and nearby organs, main bile ducts, and main blood vessels is less than 1 cm. After ablation, the authors perform a CT scan to evaluate the range of the ablation and immediate complications. The institutional review board of our hospital approved this retrospective study of existing patient data and images of our hospital. This clinical study is a retrospective study, only collecting patients' clinical data without interfering with patients'

treatment plans, which will not bring physiological risks to patients. The researchers will do their best to protect the information provided by patients from revealing personal privacy, so we hereby apply for the exemption of informed consent.

### Percutaneous MWA Technique

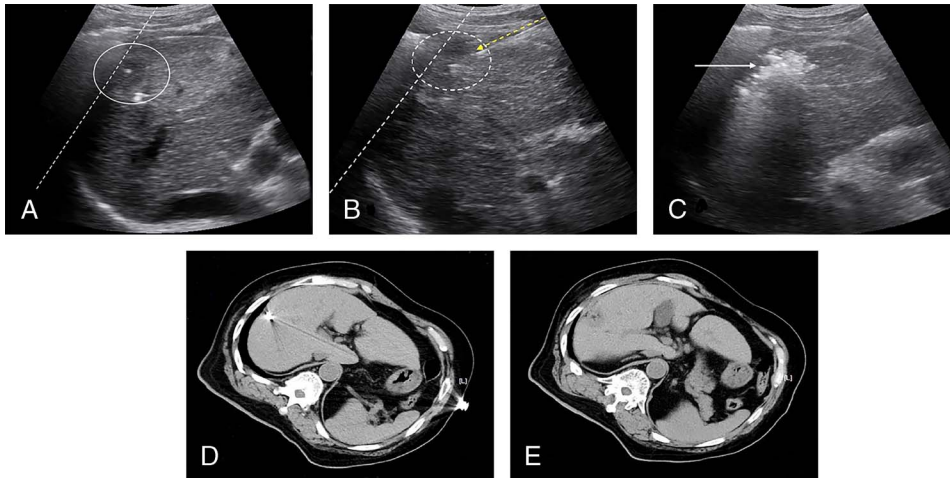
The MWA operator had 12 years of experience. Ablation was performed under US (Mindray Medical Instrument) and CT (Aquilion ONE Toshiba Medical Systems) guidance. An MTC-3C MWA system (Vison Medicine) was used, with microwave emission frequency of  $2450 \pm 50$  MHz and the adjustable continuous-wave output power of 5 to 120 W. Our study performed MWA with only one ablation antenna (MTC-3CA-2 Vison), 18 cm in length and 2 mm in diameter.

### Computed Tomography-Guided Microwave Ablation

The patient is placed supine or left lateral to expose the operation site. A CT scan was first performed to determine the puncture's entry point, direction, puncture angle, and needle depth. Anesthesia was induced with propofol and maintained. A total of 5 to 10 mL of 2% lidocaine was injected locally at the puncture point. After that, a skin incision of approximately 0.5 cm in diameter was made at the puncture site. An antenna is inserted into the tumor under CT guidance. The antenna's position is clarified using CT scans, and minor adjustments are made if necessary. Then CT scans are performed again until the antenna is inserted into the distal margin of the tumor or beyond the distal tumor 0.5 cm. Then, the ablation started. The ablation zone includes at least 0.5 to 1.0 cm of normal liver parenchyma at the margin. On withdrawal of the antenna, the antenna track was heated for 15 seconds to prevent possible tumor seeding and bleeding.

### Ultrasound/Computed Tomography-Guided Microwave Ablation

As shown in Figure 1. Patients lay supine or left lateral to expose the operation site. The US was first performed to avoid the inferior lung border and to select the entry point, path direction, and puncture angle for the puncture. Anesthesia was induced with propofol and maintained, with local injection of 5 to 10 mL of 2% lidocaine to achieve analgesia. A skin incision of approximately 0.5 cm was made at the puncture site. The antenna was inserted into the distal margin of the tumor or beyond the distal tumor 0.5 cm under US guidance. The location of the antenna was then clarified by CT scan. Then, the ablation started under the



**FIGURE 1.** Ultrasound/computed tomography-guided MWA of HCC at the top of the diaphragm. A, A portion of the tumor was found in the US. The left side of the dotted line in the picture shows the lung. B, Puncture of the nodule at one time under the guidance of ultrasound, avoiding the puncture of the lungs. The dotted arrow shows the direction of the ablation needle puncture. D, Clarification of antenna location in the tumor by CT scan. C, For such a high-risk tumor, the range of ablation can be observed in real time under the guidance of the US during MWA. E, After completing MWA, the ablation range was defined by CT scan.

guidance of the US. The next ablation steps were the same as the CT-guided MWA.

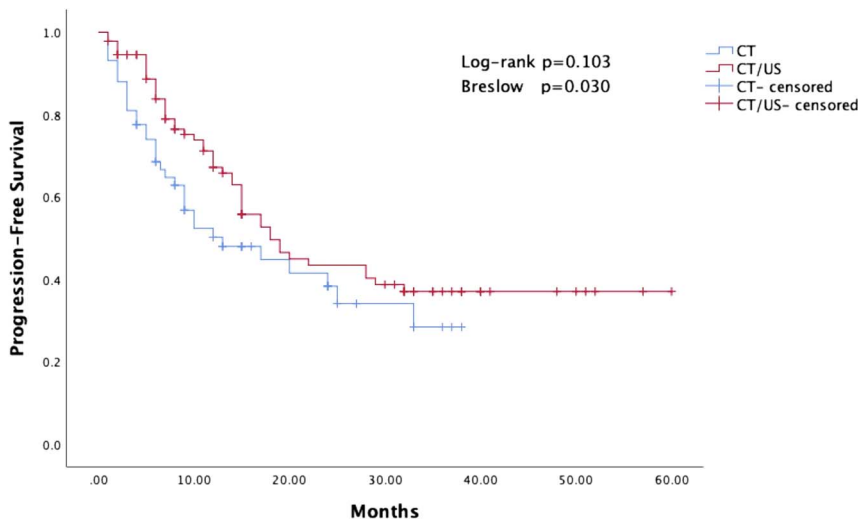
### FOLLOW-UP AND ASSESSMENT OF CLINICAL OUTCOMES

All patients were followed up until August 1, 2021. Each patient underwent an enhanced CT or MRI scan 1 month after surgery to assess the rate of complete ablation. After that, each patient was followed up with an intensive CT or MR every 3 months. Complete ablation was defined as complete tumor necrosis confirmed by contrast enhanced computed tomography or MRI 1 month after the procedure.<sup>13</sup> If the ablation zone appeared enhanced, it was defined as incomplete ablation. A second MWA treatment session was performed within 4 days after assessment. All incomplete ablated tumors achieved complete ablation after the second MWA in our study. Patients were included in the recur-

rence, and PFS statistics from the time complete ablation was achieved. Recurrence included local progression and distant recurrence in our study. Local tumor progression was defined as the appearance of any new tumor lesions at the margins of the ablation zone and distant recurrence as new distant tumor lesions that appeared in other liver segments or organs.<sup>13</sup>

### STATISTICAL ANALYSIS

Data were analyzed using IBM SPSS 26 software. The  $\chi^2$  test, Fisher exact test, and Mann-Whitney *U* test were used to compare the characteristics of the patients and clinical variables in the CT-guided and CT/US-guided groups. The Fisher exact test or  $\chi^2$  test examined the CAR, complication rate, and recurrence rate between the 2 groups. The Mann-Whitney *U* test tested the procedure time and the number of CT scan times. We used the multivariable logistic regression model to predict the association



**FIGURE 2.** Comparison of PFS between HCC lesions treated with combined US/CT guidance and US guidance alone. Short-term PFS in the combined US/CT-guided treatment group was statistically significant compared with the US-guided treatment group (log-rank  $P = 0.103$ , Breslow  $P = 0.030$ ).

**TABLE 2.** The Main Outcomes of This Study

Characteristic	CT	CT/US	P
CT scan times, median (q1–q3)	11 (8.25–14)	4 (3.75–6.0)	<0.001*
Procedure time, median (q1–q3)	40 (30–50)	30 (30–50)	0.0171*
Patients with complete ablation	49 (84.5%)	87 (94.6%)	0.0471†
Completely ablated high-risk location tumor	44 (83.0%)	76 (95.0%)	0.0347†
Recurrent patients	33 (56.9%)	47 (51.1%)	0.5063†
No. patients with overall complications	25 (43.1%)	47 (51.9%)	0.4023†
Low-grade fever	1 (1.72%)	10 (10.87%)	0.0512†
Abdominal pain	12 (20.7%)	37 (40.2%)	0.0196†
Nausea or vomiting	16 (25.81%)	7 (7.61%)	0.0026†
Pneumothorax	4 (6.9%)	0	0.0209†
Pleural effusion	2 (3.4%)	1 (1.1%)	0.5596†

\*Mann-Whitney *U* test.  
†Fisher exact test.

of image guidance and complications. Progression-free survival was calculated and described using the Kaplan-Meier method and compared with log rank (Mantel-Cox) and Breslow (generalized Wilcoxon). We used the Cox proportional hazards model and logistic regression to explore the risk factors for PFS and complete ablation. A *P* value less than 0.05 was considered statistically significant.

## RESULTS

### Characteristics of Patients

According to the inclusion criteria, 150 patients successfully underwent CT-guided MWA or CT/US-guided MWA once in our study. The characteristics of the CT/US group and the CT group of patients and their clinical variables are presented in Table 1. There were no significant differences in sex, BCLC stage, tumor size, tumor number, and high-risk location tumors between the 2 groups. Table 1 shows that the CT/US group has a lower MWA session (*P* = 0.042).

### Progression-Free Survival and Complete Ablation Rate in the 2 Groups

The Kaplan-Meier curves for the PFS of the 2 groups, presented in Figure 2, show that the 2 groups have significantly different short-term PFS (log-rank *P* = 0.103, Breslow *P* = 0.030). The complete ablation rate presented in Table 2, 87 patients in

the CT/US group were judged to be completely ablated (87/92, 94.6%). In contrast, 49 lesions of the 58 patients in the CT-guided group were assessed as having attained total complete ablation, that is, 84.5%. Thus, a significant difference was observed between these 2 groups (*P* = 0.0471). The same conclusion was obtained on the complete ablation rate for high-risk location tumors (*P* = 0.0347), based on the data presented in Table 2. The univariate and multivariate analyses of complete ablation in logistic regression are presented in Table 3 and Figure 3. We found that the CT/US-guided group has a lower risk of incomplete ablation (odds ratio [OR], 0.303; 95% confidence interval [CI], 0.095–0.970; *P* = 0.044). In addition, our study found guidance modality (hazard ratio [HR], 0.586; 95% CI, 0.368–0.934; *P* = 0.025) and BCLC stage (HR, 2.933; 95% CI, 1.678–5.127; *P* < 0.001) were risk factors for PFS (Table 4).

### Procedure Time and Number of Intraoperation CT Scan Times

The data on procedure time are presented in Table 2. A significant difference was observed between the 2 groups (*P* = 0.0171). The CT/US group had significantly fewer intraoperative CT scan times (*P* < 0.001), as shown in Table 2.

### Complications and Recurrence Rates

There were no ablation-related deaths, and major complications occurred during the study. Complications occurred in 72

**TABLE 3.** Univariate and Multivariate Analyses of Complete Ablation Patients Using Logistic Regression

Variables	Univariate	<i>P</i>	Multivariate	<i>P</i>
	OR (95% CI)		OR (95% CI)	
Guidance modality				
CT/US	1		1	
CT	0.313 (0.099–0.986)	0.047	0.303 (0.095–0.970)	0.044
BCLC stage				
A	1		1	
0	1.646 (0.491–5.517)	0.419	1.396 (0.354–5.499)	0.634
Tumor number	1.842 (0.749–4.534)	0.184	1.578 (0.509–4.896)	0.430
High-risk tumor number	1.736 (0.537–5.618)	0.357	1.268 (0.375–4.290)	0.702

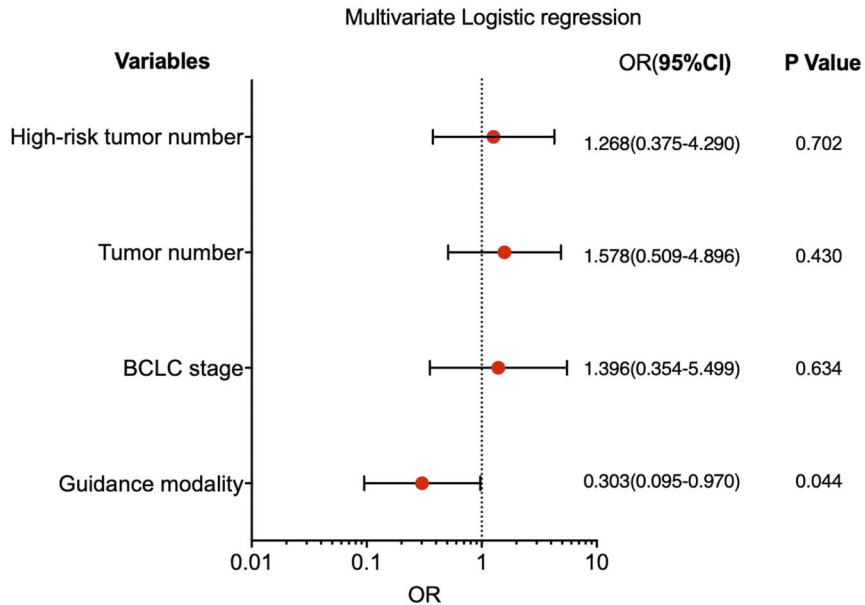


FIGURE 3. Univariate and multivariate analyses of complete ablation patients using logistic regression.

patients in this study. A total of 90 complications occurred, including abdominal pain (49/150), nausea and vomiting (23/150), low-grade fever (11/150), pneumothorax (4/150), and pleural effusion (3/150). Pneumothorax and pleural effusion were gradually absorbed within 1 week without pleural drainage. The statistics of complications and recurrence rates in the 2 groups are shown in Table 2. There was no significant difference in overall complications between the 2 groups ( $P = 0.4023$ ). Comparison of the incidence of different complications between 2 groups and the incidence of pneumothorax ( $P = 0.0209$ ), abdominal pain ( $P = 0.0196$ ), and nausea or vomiting (0.0026) were statistically different. In our multivariable logistic regression models (Fig. 4), patients who received CT-guided MWA were more likely to incident nausea and vomiting after ablation (OR, 0.221; 95% CI, 0.083–0.593;  $P = 0.003$ ). Moreover, CT/US guidance modality is the risk factor for the incident of abdominal pain after ablation (OR, 2.502; 95% CI, 1.160–5.397;  $P = 0.019$ ) (Fig. 4). The recurrence rates for the CT/US-guided and CT-guided groups were 51.1% and 56.9%, respectively. No significant differences were observed in the recurrence rate between the 2 groups ( $P = 0.5063$ ).

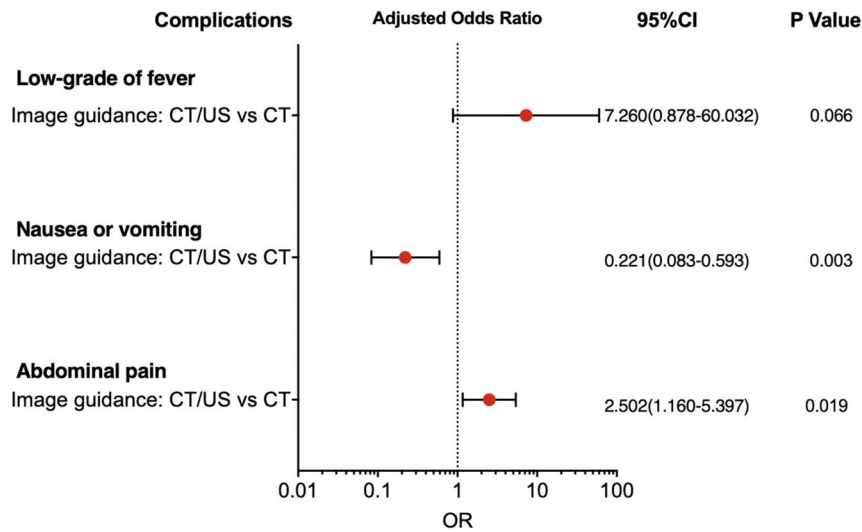
DISCUSSION

A combination of imaging modalities has been used in many disciplines in the past.<sup>13–16</sup> Thus, we evaluated the feasibility and clinical advantages of using the CT/US-guided MWA of HCC and observed that it could significantly improve safety and short-term PFS. It has been previously documented that combined imaging guidance can significantly improve accuracy and safety when puncturing lesions.<sup>17–19</sup> Furthermore, CT/US-guided puncture is not affected by the patient's respiratory movements. During ablation, a better assessment of the ablation range can be obtained because of the real-time performance of the US. Our study also found that combined imaging guidance reduced the number of CT scans and decreased the procedure time, thereby reducing the patient's radiation exposure.

In previous studies, a CAR of 94.4% to 100% was obtained for thermal ablation under the combined guidance of US/CT,<sup>9,12,18,20–22</sup> which is similar to our results. In our study, the complete ablation rate of MWA under the guidance of CT by itself was 84.5%, which is similar to the results under the CT guidance group in previously published reports.<sup>23,24</sup> Our study finds that

TABLE 4. Univariate and Multivariate Analyses of PFS in Patients Using Cox Proportional Hazards Model

Variables	Univariate		Multivariate	
	HR (95% CI)	P	HR (95% CI)	P
Guidance modality				
CT/US	1		1	
CT	0.695 (0.444–1.087)	0.111	0.586 (0.368–0.934)	0.025
BCLC stage				
A	1		1	
0	2.809 (1.673–4.717)	<0.001	2.933 (1.678–5.127)	<0.001
Tumor number	1.750 (1.145–2.674)	0.010	1.165 (0.713–1.903)	0.541
High-risk tumor number	1.412 (0.854–2.337)	0.179	1.143 (0.710–1.841)	0.582



**FIGURE 4.** Adjusted odds ratios of 2-image guidance on predicting postoperative complications. The OR does not exist for pneumothorax and pleural effusion due to limited cases presented included.

the success rate of a single ablation session is higher for combined imaging-guided ablation than for CT-guided ablation alone. Yasunori Minami et al<sup>25</sup> also reported the same result. The reason for easier access to complete ablation of the tumor may be related to the advantages of puncture guidance and intraoperative ablation with combined guidance that we have mentioned previously. In another retrospective study on thermal ablation of the hepatic dome, the low recurrence rate in the combined CT/US guidance method was confirmed.<sup>26</sup> However, their study did not indicate a statistical difference in the recurrence rate between the 2 groups. In addition, our study found no statistically significant recurrence rates in the 2 groups after complete ablation was achieved. Jing Wu et al<sup>27</sup> and Jinhai Huo et al<sup>28</sup> have previously reported no statistical difference in PFS when comparing the US and CT-guided tumor MWA. Our study found that posttreatment short-term PFS was statistically different. After incomplete ablation, we believe that tumors may undergo dedifferentiation and show higher aggressiveness. This aggressiveness makes patients who fail the first ablation more likely to progress early.

When performing MWA, it usually makes the ablation edge at least 10 mm around the lesion to form a circular nonenhanced area. However, for some lesions in high-risk areas, such as the top of the diaphragm, proximal sac, intestinal duct, main vessels, main bile duct, gallbladder, and other high-risk areas. Sometimes, such criteria are not met. The previous study has also demonstrated the advantages of combined CT/US guidance over single CT guidance for abating tumors in the hepatic dome.<sup>26</sup> However, they did not do a statistical analysis of the complete ablation rates of the 2 groups. Our study further found that the combined guidance group had a higher complete ablation rate of high-risk location tumors. This result demonstrates that the puncture advantage of combined guidance and the ablation advantage remain when targeting high-risk site lesions.

It is a fact that CT causes radiation exposure that affects patients' health.<sup>29,30</sup> Many studies reported that CT-guided ablation requires constant CT scans to determine the location of the ablation antenna, resulting in the accumulation of radiation dosage.<sup>12,17,18,20,27,31</sup> Radiation exposure should be reduced as much as possible during ablation. Considering the real-time performance of the US and the high detection ability of CT, the combination would reduce the number of times of repeated CT scans during puncture and ablation. Therefore, CT/US-guided ablation

can also reduce the procedure time. Our study found that although there was no difference in the incidence of overall complications, the CT/US group had a lower incidence of pneumothorax. Xuefeng Kan et al<sup>26</sup> also reported the same differences. This result considers that for site-specific tumors, the combined guidance group can avoid penetration to the lower lung margin during puncture and thus pneumothorax because of the assistance of the US. The CT-guided MWA group was more prone to nausea and vomiting after ablation. We consider that this is related to the longer operative time, therefore longer application of anesthetic drugs in the CT-guided group. An interesting finding in our study was that the incidence of abdominal pain in the CT/US-guided MWA was significantly greater than that of the other group. This result is the opposite of the conclusion reached in a previous article.<sup>28</sup> The reason is not clear. More studies are needed to confirm this conclusion. These results further confirm the safety of combined CT/US guidance.

In conclusion, we demonstrated that the CT combined with US guidance has a better clinical benefit than the CT guidance alone in HCC MWA. We found that the CT/US combined guidance can significantly improve CAR and short-term PFS and shorten procedure time by comparing the 2 groups. Computed tomography/ultrasound-guided MWA can also reduce intraoperative radiation exposure and the incidence rate of pneumothorax. Our study had certain limitations. First, this was a retrospective study and used a nonrandomized design. The guidance options for MWA were determined based on the preference of the MWA operator, and all patients are from our one institution. Therefore, a large randomized controlled trial is needed to validate the results. Second, patients with contrast enhanced ultrasound-guided MWA were not included in this study. We can conduct a comparative study on the clinical efficacy of MWA under the guidance of CT/US, CT, and contrast enhanced ultrasound; this should be investigated in future studies.

### CONCLUSIONS

To our knowledge, this is a rare retrospective study with large sample size and extended follow-up to assess the clinical efficacy of CT/US-guided MWA. Our findings will contribute to the choice of imaging guidance modality and patient selection in MWA and improve the clinical efficacy and safety of HCC MWA.

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