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Original Article

Risk factors of liver dysfunction induced by microwave ablation in patients with hepatocellular carcinoma

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Abstract: Objective: To investigate the risk factors of liver function damage induced by microwave ablation (MWA) in patients with hepatocellular carcinoma (HCC). Methods: We retrospectively reviewed the liver function of 498 patients with HCC undergoing MWA treatment. The dynamic changes of liver enzymes and Child-Pugh scores were observed. The potential risk factors, including the relative position between the tumor and portal vein (PV), tumor numbers, ablation volumes, Child-Pugh classifications, platelet, APRI and MELD scores, were analyzed. Results: 13.86% (69/498) patients suffered from liver function damage, that is, having an increase of two in Child-Pugh score three days after MWA. The incidences of liver dysfunction of the patients with tumors close to PV, more than three tumors, ablation volumes larger than or equal to 22.5 cm^3, Child-Pugh classification B, APRI > 1.6, MELD > 30 or PLT < 110 × 10^9/L were 53.85%, 46.15%, 20.60%, 24.24%, 31.53%, 22.55% or 18.92%, respectively, all of which are much higher than those of patients without the aforementioned characteristics. Conclusions: MWA can cause a transient deterioration of liver function. Patients with tumors close to PV, large number of tumors or large ablation volumes may present a great fluctuation of liver enzymes and an aggravation of liver dysfunction. In addition, poor liver reserve function is a risk factor of liver function damage, but not the elevation of liver enzymes after MWA.

Keywords: Microwave ablation, liver dysfunction, hepatocellular carcinoma, risk factors

Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancy around the world [1]. Approximately, up to one million new liver cancer cases are diagnosed and about 745,500 people die of HCC-related diseases each year, making it already the second commonest cause of cancer-related mortality [2].

Thermal ablation techniques, especially percutaneous radiofrequency ablation (RFA) and microwave ablation (MWA), are widely used in the treatment of HCC in recent years [3-7] because of their minimal invasion and superior treatment efficacy. However, ablation of tumors usually accompanies with the deterioration of liver function [8, 9]. Previous studies showed that liver function damage after RFA is related to the location of tumors, level of platelet and Child-Pugh score [8, 10, 11]. Compared with RFA, MWA have a higher output power and larger ablation volume and therefore may increase the possibility of liver dysfunction [12, 13]. The dynamic changes of liver function induced by MWA in patients with HCC, however, have not been well studied. In China, however, most of the patients are with poor liver reserve function due to the chronic viral hepatitis and liver cirrhosis [1, 2]. These patients, hence, are prone to suffer from liver dysfunction after thermal ablation. To prevent from the possible liver dysfunction and further complications, it is of paramount importance to understand their related factors.

In the present study we monitored the changes of liver function after MWA. A total of seven fac-

Table 1. Baseline characteristics of the patients in this study before MWA ablation

Parameters	Value
Number of patients	498
Total number of tumors	721
Sex (Male/Female)	374/124
Age	59.56 ± 9.07
Etiology	
Hepatitis B virus	410
Hepatitis C virus	55
Alcohol	9
Others	24
Child-Pugh classification	
A	432
B	66
ALB (g/L)	39.84 ± 5.99
ALT (U/L)	32.68 ± 22.01
AST (U/L)	36.14 ± 22.54
ALP (U/L)	87.17 ± 41.75
γ-GGT (U/L)	76.39 ± 119.15
TBIL (μmol/L)	18.87 ± 10.40
PLT (10^9/L)	108.16 ± 58.66
Relative position between the tumor and PV	
Far away	407
Close to the third branch	72
Close to the second branch	13
Close to the first branch	6
Number of tumors (1/2-3/> 3)	336/149/13
APRI	1.17 ± 1.07
Size of the tumors (cm)	2.39 ± 0.82

serum albumin (ALB), alanine transaminase (ALT), aspartate aminotransferase (AST), alkalinephosphatase (ALP), gamma-glutamyltranspeptidase (γ-GGT), serum total bilirubin (TBIL), blood platelet count (PLT), aspartate aminotransferase-to-platelet ratio index (APRI).

tors, including the relative position between the tumor and PV, tumor numbers, ablation volumes, Child-Pugh classification, PLT, APRI and MELD scores, were included in this study to explore the reasons of the occurrence of liver dysfunction.

Methods

Patients

This retrospective study was approved by Tianjin Third Central Hospital Institutional Review Board. All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The informed consents of the patients were waived. All the treatments were performed in accordance with relevant guidelines and regulations. Patients selected in this study obey the following inclusion criteria: (1) they were diagnosed with HCC and underwent MWA; (2) the diameters of their nodules were ≤ 5 cm; (3) the number of the nodules was ≤ 5; (4) they did not suffer from portal thrombus or extrahepatic metastases; (5) they had liver cirrhosis and a liver function of Child-Pugh classification A or B; (6) the level of platelet counts was ≥ 50 × 10^9/L or the international normalized ratio was ≤ 1.7; (7) did not receive any other invasive treatment, such as PEI, TACE, RFA, during preoperative and postoperative period and (8) they did not suffer from non-liver related serious complications after MWA. Patients were excluded from the study for the following reasons: (1) with a tumor > 5 cm in size or with > 5 tumors; (2) undergoing other invasive treatment during preoperative or postoperative period; (3) with serious complications which may have an effect on liver function damage. A total of 498 patients were included in this study (**Table 1**). All of the diagnoses were reconfirmed by ultrasound guided percutaneous biopsy.

MWA ablation

MTC-3 microwave therapy instrument (Forsea Microwave & Electronic Research Institute, Nanjing, China) with a frequency of 2450 MHz and an output power of 40-80 W was used for MWA therapy. The diameter of the cooling unipolar needle was 16-guage and the length of it is 15 cm. All of the MWA procedures were performed percutaneously by using the ultrasound systems of Philips IU-22 (Philips, Bothell, WA, USA) with a frequency of 1-5 MHz convex array probe under the real-time US guidance. In order to achieve complete necrosis of a tumor, the radius of ablation volume was 0.5 cm larger than that of the tumor.

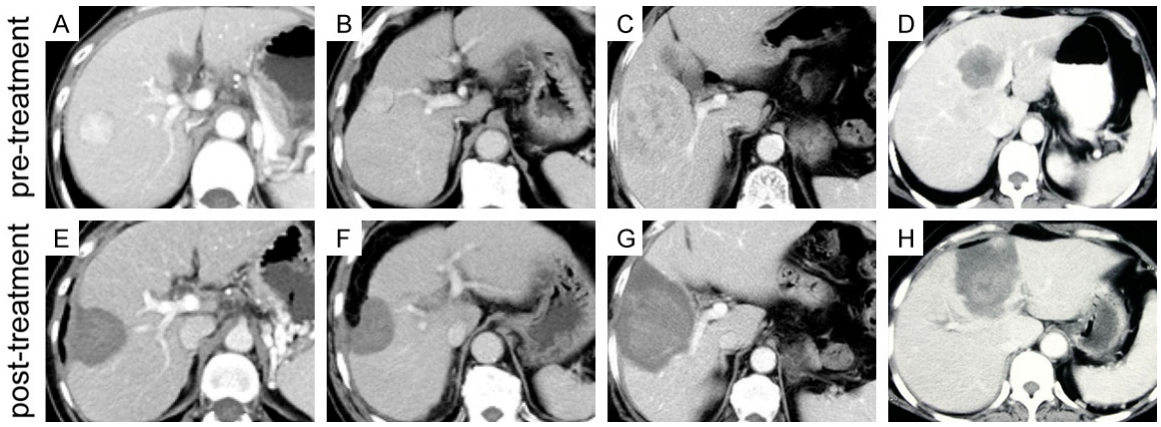

Figure 1. Relative position between the tumor and portal vein. A. The tumor far away from portal vein before treatment. B. The tumor close to the third branch of portal vein before treatment. C. The tumor close to the second branch of portal vein before treatment. D. The tumor close to the first branch of portal vein before treatment. E. The tumor far away from portal vein after treatment. F. The tumor close to the third branch of portal vein after treatment. G. The tumor close to the second branch of portal vein after treatment. H. The tumor close to the first branch of portal vein after treatment.

Follow-up

To confirm the curative effect of MWA, enhanced computed tomogram (CT) or magnetic resonance imaging (MRI) scan was performed one month after MWA. Complete tumor ablation was confirmed when the postoperative hypoattenuation/hypointensities was in all the phases of the CECT or CEMRI. Blood tests for liver function, complete blood count and prothrombin time (PT) were routinely performed along with imaging.

Assessment of liver function and data collection

The size of tumors, number of tumors, relative position between the tumor and portal vein (PV), blood platelet count, serum albumin (ALB), alanine transaminase (ALT), aspartate aminotransferase (AST), alkalinephosphatase (ALP), gamma-glutamyltranspeptidase (γ-GGT), serum total bilirubin (TBIL), Child-Pugh classification, MELD score, total ablation volume and aspartate aminotransferase-to-platelet ratio index (APRI) were collected. The laboratory test was performed and Child-pugh scores were collected before, 3 days after and 1 month after MWA. Based on the relative position between the tumor and PV, the tumors of the patients were divided into four groups, (1) far away from PV; (2) close to the third branch of PV (< 5 mm); (3) close to the second branch of PV (< 5 mm); (4) close to the first branch of PV (< 5 mm). If a tumor was near by the furcation of portal vein, the tumor was classified to the group with the larger branch. Deterioration of liver function was defined as an increase of Child-Pugh score by two three days after MWA therapy.

Statistics

Continuous variables are shown as mean ± standard error. Categorical variables are presented by frequencies and percentages. Comparisons between liver function parameters at different times were performed using the repeated measures analysis of variance or paired Student's t-test. The Receiver Operating Characteristic Curve (ROC) was used to determine the cut-of value. A *p*-value of less than 0.05 indicated a significant difference. All the statistical analysis was conducted using SPSS package.

Results

All the patients were successfully treated by percutaneous microwave ablation without any procedure-related death. 721 tumors were included in this study. Among them, 156 tumors were close to the PV and the rest 565 tumors were far away from PV. Complete response was achieved in 409 (98.08%) of 417 patients with tumors far away from the PV and in 89 (95.70%) of 93 patients with tumors close to a branch of the PV (**Figure 1**), respectively.

Three days after MWA, 91 patients with a classification of Child-Pugh A shifted to B, 12 pa-

Table 2. Changes of liver function indicators before, three days and one month after MWA

	Before	Three days after	One month after	*P* value
ALB	39.84 ± 5.99	36.40 ± 4.71	40.82 ± 6.61	< 0.001
ALT	32.68 ± 22.01	196.51 ± 197.40	37.89 ± 34.07	< 0.001
AST	36.14 ± 22.54	221.60 ± 203.60	46.74 ± 37.12	< 0.001
ALP	87.17 ± 41.75	82.78 ± 42.10	90.07 ± 69.72	0.189
γ-GGT	76.39 ± 119.15	72.45 ± 103.09	80.27 ± 90.40	0.555
TBIL	18.87 ± 10.40	26.42 ± 15.31	21.71 ± 15.69	< 0.001

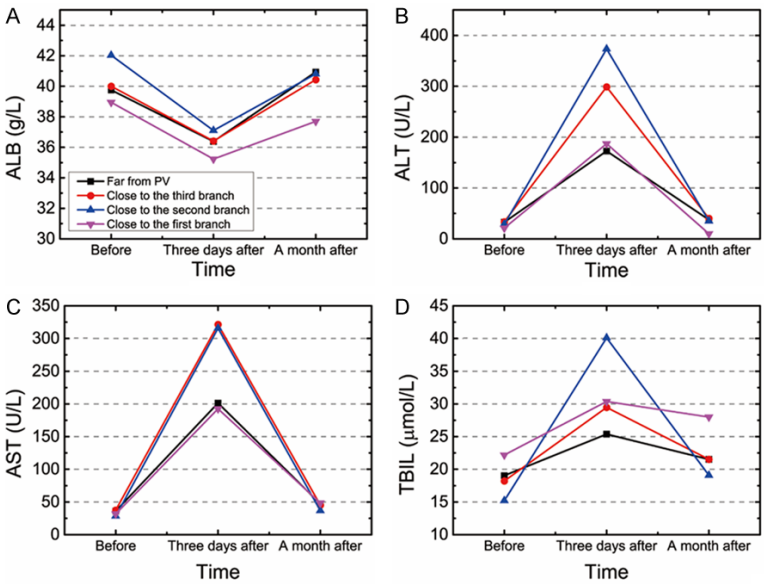

Figure 2. Effects of the relative position between the tumor and PV on the dynamic changes of liver biochemical laboratory values three days after and one month after MWA.

tients from B to C and one patient from A to C. A total of 69 patients suffer from liver dysfunction, that is, have an increase of two in Child-Pugh score three days after MWA.

The changes of liver function indicators were shown in **Table 2**. Large fluctuations in levels of ALB, ALT, AST and TBIL were observed three days after treatment, while the concentrations of ALP and γ-GGT were relative stable.

Effects of the relative position between the tumor and PV on liver function

The incidences of liver dysfunction of the patients with tumors far away from PV, close to the third branch, the second branch and the first branch of PV were 9.58% (39/407), 29.17% (21/72), 53.85% (7/13) and 33.33% (2/6), respectively ($P < 0.001$). The time evolutions of liver biochemical laboratory values, including ALB, ALT, AST and TBIL were shown in **Figure 2**. The levels of ALT three days after MWA of patients with tumors far away from PV, close to the third branch, the second branch and the first branch of PV increased by 139.11 ± 163.17, 265.28 ± 301.36, 344.55 ± 234.96 and 165.83 ± 92.74 U/L ($P < 0.001$), respectively, of AST, 165.15 ± 178.12, 283.91 ± 278.93, 287.31 ± 300.39 and 160.76 ± 91.17 U/L ($P < 0.001$), respectively, and of TBIL, 6.27 ± 11.05, 11.25 ± 12.21, 24.88 ± 27.58 and 8.17 ± 8.59 (μmol/L) ($P < 0.001$), respectively.

Effects of the tumor numbers on liver function

The patients with more than three tumors had an incidence of 46.15% for liver dysfunction, higher than those with two or three tumors (20.81%) and with only a tumor (9.52%). Time evolutions of liver biochemical laboratory values were shown in **Figure 3**. Three days after MWA, the levels of ALT increased by 131.01 ± 148.45, 204.03 ± 2210.79 U/L and 521.00 ± 513.08 U/L respectively in patients with one, two or three and more than three tumor(s) ($P < 0.001$). The levels of AST increased by 153.46 ± 171.48, 225.96 ± 193.25, 548.40 ± 487.81 U/L, respectively ($P < 0.001$) and of TBIL, 6.31 ± 11.98, 9.04 ± 11.50 and 20.37 ± 19.60 (μmol/L), respectively ($P < 0.001$). The changes of the concentrations of ALB of the three groups had no statistically significance.

Effects of the ablation volumes on liver function

ROC curve was adopted to find out the cut-off value of ablation volumes, i.e. 22.5 cm^3. In this study, 265 patients had ablation volumes less than 22.5 cm^3 and 233 patients were with

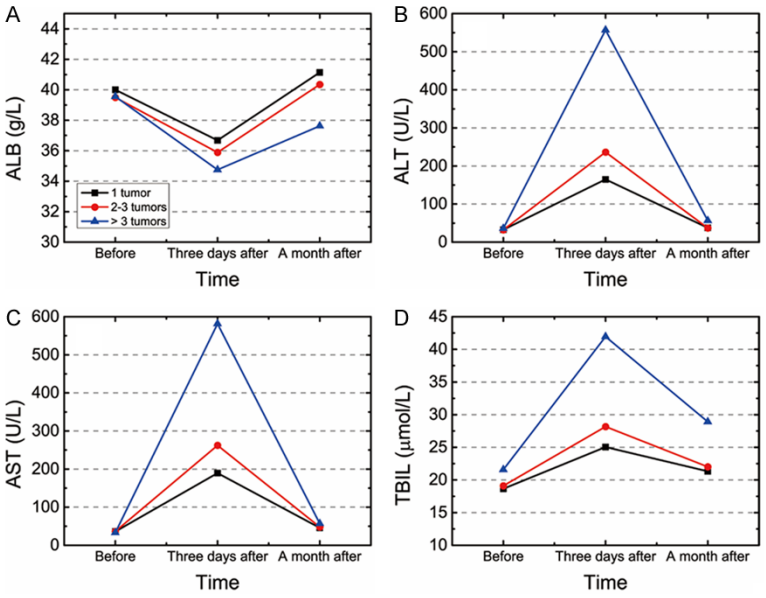

Figure 3. Effects of the tumor numbers on the dynamic changes of liver biochemical laboratory values three days after and one month after MWA.

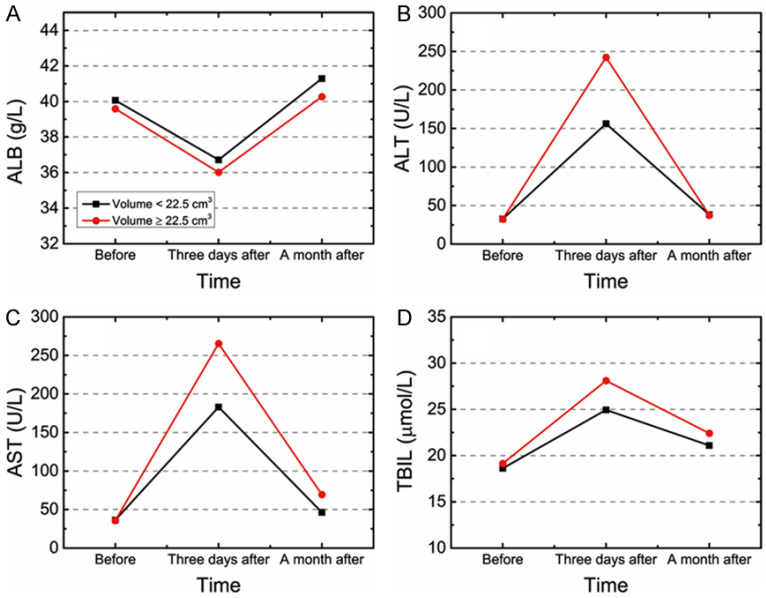

Figure 4. Effects of the ablation volumes on the dynamic changes of liver biochemical laboratory values three days after and one month after MWA.

ablation volumes lager than or equal to 22.5 cm^3. Liver dysfunction incidences in patients with small and large ablation volumes were 7.92% and 20.60%, respectively, ($P < 0.001$). The time evolutions of liver biochemical laboratory values for two groups were shown in **Figure 4**. The differences between the two groups in the elevated levels of ALT, AST and TBIL were statistically significant (< 22.5 cm^3 vs ≥ 22.5 cm^3: 122.81 ± 152.82 vs 208.79 ± 230.22 U/L for ALT, $P < 0.001$; 146.56 ± 177.14 vs 229.70 ± 221.60 U/L for AST, $P < 0.001$; and 6.31 ± 10.08 vs 8.86 ± 14.31 μmol/L for TBIL, $P=0.024$). The elevated levels of ALB in patients with ablation volumes < 22.5 cm^3 or ≥ 22.5 cm^3 were 3.33 ± 4.80 and 3.72 ± 4.67 g/L, respectively ($P=0.364$).

Effects of the Child-Pugh classification before MWA on liver function

The incidence of patients with Child-Pugh classification B suffering from liver dysfunction was 24.24% (16 of 66), much higher than that of patients with classification A (53 of 432, 12.17%, $P=0.009$). The time evolutions of liver biochemical laboratory values for the two groups were shown in **Figure 5**. Three days after MWA, the levels of ALB decreased from 41.18 ± 4.78 to 37.17 ± 4.24 g/L in patients with Child-Pugh classification A and from 31.64 ± 4.84 to 31.40 ± 3.82 g/L in patients with classification B. The decreased levels of ALB in the classification A group was greater than B group (3.99 ± 4.56 vs 0.46 ± 4.77 g/L, $P < 0.001$). The increased level of ALT was 175.23 ± 203.66 U/L three days after MWA in the classification A group, also greater than that in the classification B group (83.23 ± 125.08 U/L), $P < 0.001$. The elevated concentrations of AST and TBIL were comparable in two groups (the classification A vs classification B group: 188.10 ± 199.67 vs 168.17 ± 226.25 U/L, $P=0.459$, for AST; 7.65 ± 11.80 vs 6.47 ± 15.24 μmol/L, $P=0.467$, for TBIL).

Effects of APRI on liver function

Patients were divided into three groups according to the cut-off values of APRI, namely, ≤ 0.8,

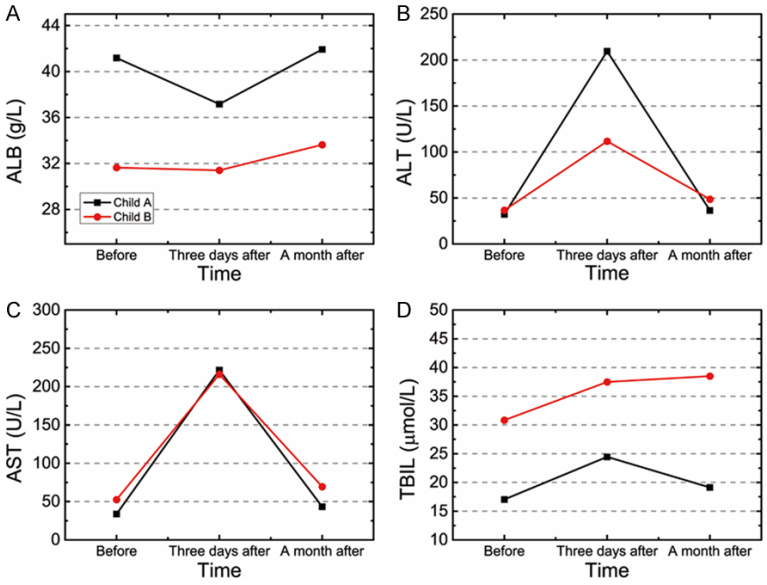

Figure 5. Effects of the Child-Pugh classification on the dynamic changes of liver biochemical laboratory values three days after and one month after MWA.

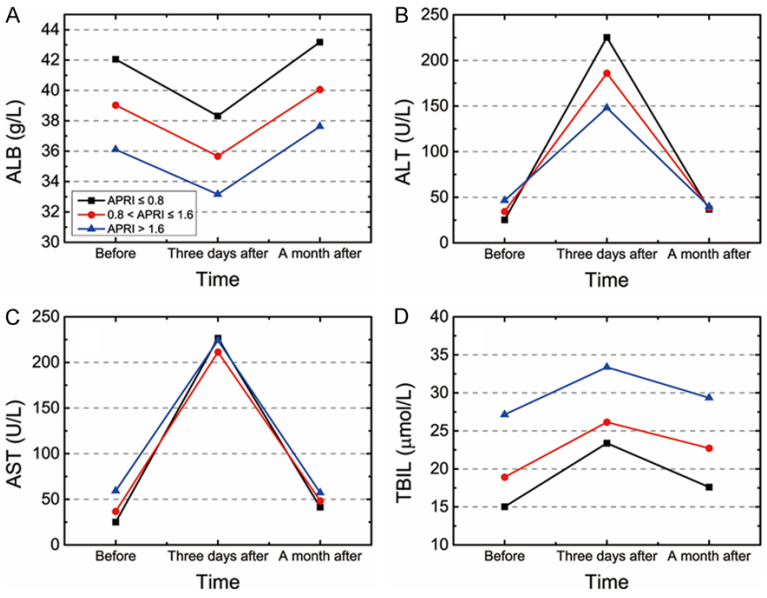

Figure 6. Effects of APRI on the dynamic changes of liver biochemical laboratory values three days after and one month after MWA.

0.8 to 1.6 and > 1.6. The numbers of patients in the three groups were 241, 146 and 111, respectively. The possibilities of liver dysfunction were related to the APRI and the corresponding liver dysfunction rates for the three groups were 6.44%, 12.33% and 31.53%, respectively (P < 0.001). The changes of the liver biochemical laboratory values of the three groups before and after MWA treatment were shown in **Figure 6**. All the fluctuations in ALB, AST and TBIL, except in ALT, had no statistically significance. The smaller the APRI is, the more the concentration of ALT increases, i.e., 199.10 ± 225.55 U/L when APRI ≤ 0.8, 150.29 ± 169.68 U/L when APRI between 0.8 to 1.6, and 101.50 ± 142.62U/L when APRI > 1.6.

Effects of PLT on liver function

According to the ROC curve, the cut-off of PLT was found to be 110 × 10^9/L. The numbers of patients with PLT < 110 × 10^9/L and ≥ 110 × 10^9/L were 287 and 211, respectively. The incidence of liver dysfunction was 18.82% in patients with PLT levels < 110 × 10^9/L, significant higher than that in patients with PLT ≥ 110 × 10^9/L (7.11%, P < 0.001). The time evolutions of liver biochemical laboratory values for the two groups were shown in **Figure 7**. Similar to the results of APRI, the changes of ALB, AST and TBIL were comparable between the two groups. The patients with lower PLT, however, had a larger fluctuation of ALT than those with PLT ≥ 110 × 10^9/L (189.28 ± 211.05 vs 143.74 ± 184.85 (10^9/L), P=0.011).

Effects of MELD scores on liver function

The patients were classified into three groups according to the cut-off values of MELD score, namely, MELD score < 25, 25 ≤ MELD score < 30, and MELD score ≥ 30. The numbers of the patients of the three groups were 139, 257 and 102, respectively. The corresponding incidences of liver dysfunction were 5.76%, 14.79% and 22.55% (p < 0.001), respectively. The incidence

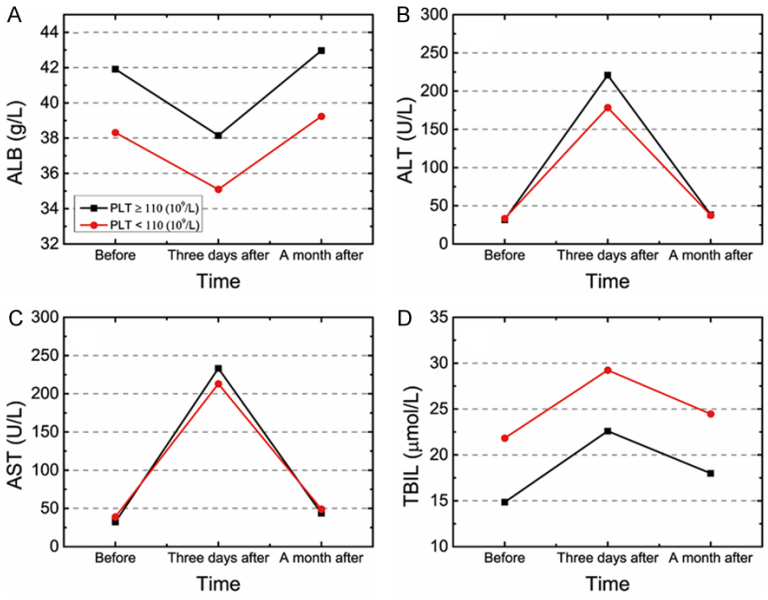

Figure 7. Effects of PLT on the dynamic changes of liver biochemical laboratory values three days after and one month after MWA.

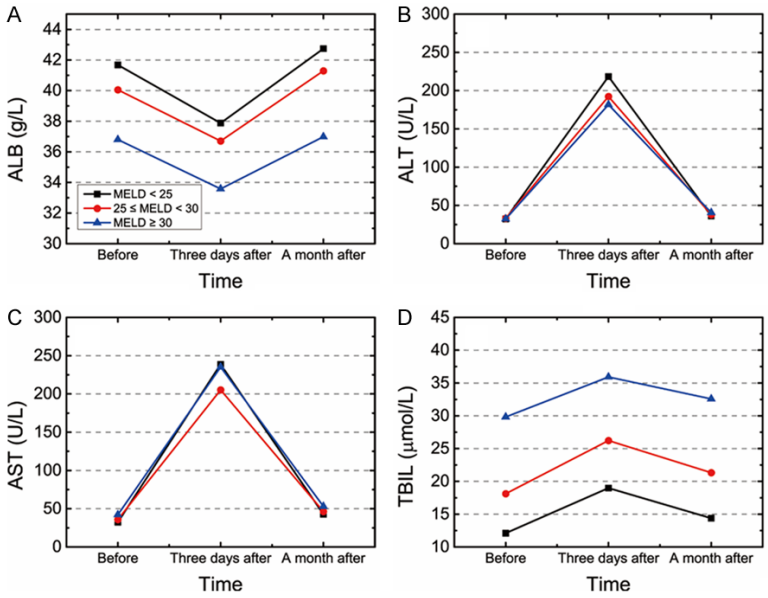

Figure 8. Effects of the MELD scores on the dynamic changes of liver biochemical laboratory values three days after and one month after MWA.

of liver dysfunction of patients with MELD scores ≥ 30 was about 4 times of that of patients with MELD scores < 25. The time evolutions of the liver biochemical laboratory values for the three groups were shown in **Figure 8**. All the changes of liver biochemical laboratory values before and after MWA among the above-mentioned three groups were not statistically significant (ALB, P=0.242; ALT, p=0.288; AST, p=0.227 and TBIL, p=0.740).

Case report

This patient was a 72-year-old woman with hepatitis C virus related liver cirrhosis. She was admitted to our institution for the treatment of three recurrences HCC tumors with diameters of 2.6, 2.3 and 1.5 cm, one of which closed to the third branch of PV. The patient was treated by the TACE and MWA therapy for HCC several months ago. The laboratory data showed that the levels of PLT, ALB, ALT, AST, ALP, γ-GGT and TBIL of the patients were 69 (10^9/L), 29.6 g/L, 34 U/L, 49 U/L, 71 U/L, 105 U/L and 26.8 μmol/L, respectively. Her liver function was evaluated as Child-Pugh classification B according to the corresponding criteria. The calculated APRI was 1.76 and the MELD score was 31.98.

MWA was performed strictly in accordance with the procedure detailed in the method section. The patient suffered from serious liver function damage and hepatic coma syndromes. Laboratory testing of blood revealed the following levels: blood ammonia, 57 μmol/L; PLT, 59 (10^9/L); ALB, 26.3 g/L; ALT, 873 U/L; AST, 1760 U/L; ALP, 101 U/L; GGT, 117 U/L; TBIL, 84.2 μmol/L, respectively. The Child-Pugh classification of the patient shifted from B to C. CT scan showed a large volume ascites. Branched chain amino acid (BCAA) and ornithine aspartate were used to reduce the blood ammonia. Drainage of ascites was admitted. Liver protecting and prophylactic antibiotics therapy were performed. Two weeks later, the physical condition of the patient was improved with the symptoms of hepatic coma and ascites disappeared. The

concentrations of ALT and AST recovered to normal values. The patient was discharged with hypoproteinemia and hyperbilirubinemia because of her claim. Eventually, the patient died due to the multiple organ failure 5 months after MWA.

Discussion

Nowadays, the demand for security of thermal ablation is getting higher and higher. The corresponding risk factors of some of complications, therefore, were clarified in previous studies [14-16]. However, due to the relatively low incidence of serious liver dysfunction, the potential thermal damage of liver function mentioned in previous studies [8, 11, 17], is usually ignored in practice. The aim of this study was to investigate effects of MWA on liver function and the risk factors of liver function damage.

Our results show that the concentration of ALT, AST and TBIL increased while the level of ALB decreased three days after treatment, all of which recovered within one month except for TBIL. 13.86% (69/498) patients suffered from liver function damage. The incidence of liver dysfunction in this study is lower than that in the studies of Koda et al. and Li et al. [17, 18], in which the incidences were 25% and 36%, respectively. The low incidence of liver function damage in our study may be on account of good liver reserve functions of the patients. Moreover, we investigated the risk factors of liver function damage systematically.

The results of our study demonstrate that the tumor-related local factors have effects on liver enzymes and reserve function. Patients with tumor(s) close to PV, large number of tumors or large ablation volume have significant fluctuations in liver enzymes and are prone to suffer from liver function damage. We suggest that there are two reasons resulting in the aggravating liver function damage from above three factors. Firstly, the heat produced by MWA may cause injury of the normal hepatic parenchyma surrounding the tumor. With the increase in tumor numbers or ablation volume, more parenchyma is ablated and more serious liver damage may happen. Our conclusion is consistent with the results of Cizginer et al. [19], which confirmed that the elevated aminotransferase levels are correlated with the ablation volume. Secondly, the heat produced by microwave antenna is delivered to liver parenchyma away from the ablation area and then harm the tissues. This damage usually happens when the tumor near a large vessel is ablated, as firstly reported by Jiang et al. [8]. Liu et al. [20] also found that thermal ablation for liver cancers adjacent to large vessels results in transiently damage of liver function. The results of this study also suggest that the larger portal vein the tumor is close to, the more seriously liver function is damaged. Besides, the loss of heat may increase the risk of inadequate tumor ablation [21]. In order to achieve complete necrosis of tumor, more liver parenchyma may be ablated. Hence, the incidence of liver damage will further increase.

Liver reserve function related factors have a great influence on the increase in Child-Pugh score instead of liver laboratory data. Patients with liver function of Child-Pugh classification B, high APRI, low level of PLT or large MELD scores have a high possibility of liver dysfunction. The effects of Child-Pugh score and PLT on liver function have been explored in previous studies. Li et al. [18] and Kuroda et al. [11] reported that patients with Child-Pugh scores larger than 8 are at the high risk of the aggravation of liver dysfunction after RFA. Lee et al. [10] demonstrated that thrombocytopenia is a critical parameter to predict the deterioration of liver function after RFA. These results were also confirmed by this study. However, none of the previous studies, to our best extent, mentioned the effects of APRI and MELD scores on liver dysfunction. APRI, an indicator of liver stiffness, can reflect the degree of liver cirrhosis directly [22, 23]. MELD scores is a system assessing the severity of chronic liver disease, eliminating the effects of two subjective variables, portosystemic encephalopathy and severity of ascites [24]. Both of APRI and MELD are related to liver dysfunction as depicted in this study.

This study has several limitations. Firstly, we did not take the influence of indocyanine green retention rate into account. Secondly, Chronic liver diseases may impact the results of this study, but we did not discuss the long-term change of hepatic function after the percutaneous tumor ablation. In future, a long-term case-control study may be helpful in accurately predicting the effects of MWA on liver function.

Conclusion

MWA is minimally invasive and with a relative low incidence of liver function damage in the treatment of HCC. Patients with tumors close to PV, large numbers of tumors and large ablation volumes may present a great fluctuation of liver enzymes and an aggravation of liver dysfunction. In addition, serious liver dysfunction is more likely to happen in patients with poor liver reserve function.

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Disclosure of conflict of interest

None.

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References

[1] Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo MS, Parkin DM, Forman D, Bran F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015; 136: E359-E386.

[2] Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA: Cancer J Clin 2012; 65: 87-108.

[3] Shi J, Sun Q, Wang Y, Jing X, Ding J, Yuan Q, Ren C, Shan S, Wang Y, Du Z. Comparison of microwave ablation and surgical resection for treatment of hepatocellular carcinomas conforming to Milan criteria. J Gastroen Hepatol 2014; 29: 1500-1507.

[4] Yang W, Yan K, Goldberg SN, Ahmed M, Lee JC, Wu W, Zhang ZY, Wang S, Chen MH. Ten-year survival of hepatocellular carcinoma patients undergoing radiofrequency ablation as a first-line treatment. World J Gastroenterol 2016; 22: 2993-3005.

[5] Dietrich CF, Lorentzen T, Appelbaum L, Buscarini E, Cantisani V, Correas JM, Cui XW, Onofrio MD, Gilja OH, Hocke M. EFSUMB guidelines on interventional ultrasound (INVUS), Part III. Ultraschall Med 2016; 37: E1-E32.

[6] Yu J, Yu XL, Han ZY, Cheng ZG, Liu FY, Zhai HY, Mu MJ, Liu YM, Liang P. Percutaneous cooled-probe microwave versus radiofrequency ablation in early-stage hepatocellular carcinoma: a phase III randomised controlled trial. Gut 2017; 66: 1172-1173.

[7] Ding J, Jing X, Liu J, Wang Y, Wang F, Du Z. Complications of thermal ablation of hepatic tumours: comparison of radiofrequency and microwave ablative techniques. Clin Radiol 2013; 68: 608-615.

[8] Jiang K, Dong J, Zhang W, Liu Y, Su M, Zhao X, Wang J, Yao M, Huang ZM. Effect of one-off complete tumor radiofrequency ablation on liver function and postoperative complication in small hepatocellular carcinoma. Eur J Surg Oncol 2014; 40: 576-583.

[9] Xiong L, Zhang L, Ma J, Li J. Efficacy of radiofrequency ablation plus hepatic arterial chemoembolization in primary hepatic carcinoma and its effect on serum markers. Int J Clin Exp Med 2017; 10: 14076-14082.

[10] Lee HS, Park SY, Kim SK, Kweon YO, Tak WY, Cho CM, Jeon SW, Jung MK, Park HG, Lee DW, Choi SY. Thrombocytopenia represents a risk for deterioration of liver function after radiofrequency ablation in patients with hepatocellular carcinoma. Clin Mol Hepatol 2012; 18: 302-308.

[11] Kuroda H, Kasai K, Kakisaka K, Yasumi Y, Kataoka K, Ushio A, Miyamoto Y, Sawara K, Oikawa K, Kondo K. Changes in liver function parameters after percutaneous radiofrequency ablation therapy in patients with hepatocellular carcinoma. Hepatol Res 2010; 40: 550-554.

[12] Poulou LS, Botsa E, Thanou I, Ziakas PD, Thanos L. Percutaneous microwave ablation vs radiofrequency ablation in the treatment of hepatocellular carcinoma. World J Hepatol 2015; 7: 1054-1063.

[13] Riad MA, Elsawy AA, Elbadry AM, Ahmed LM. Study of therapeutic efficacy of percutaneous radiofrequency ablation versus percutaneous microwave ablation for hepatocellular carcinoma. Tanta Med J 2017; 45: 8-13.

[14] Yang W, Yan K, Wu GX, Wu W, Fu Y, Lee JC, Zhang ZY, Wang S, Chen M. Radiofrequency ablation of hepatocellular carcinoma in difficult locations: strategies and long-term outcomes. World J Gastroenterol 2015; 21: 1554-1566.

[15] Li M, Yu X, Liang P, Dong B, Liu F. Ultrasound-guided percutaneous microwave ablation for hepatic malignancy adjacent to the gallbladder. Int J Hyperthermia 2015; 31: 579-587.

[16] Kang TW, Rhim H, Lee MW, Kim Y, Choi D, Lee WJ, Lee HK. Radiofrequency ablation for hepatocellular carcinoma abutting the diaphragm: comparison of effects of thermal protection and therapeutic efficacy. Am J Roentgenol 2011; 196: 907-913.

[17] Koda M, Ueki M, Maeda Y, Mimura K, Okamoto K, Matsunaga Y, Kawakami M, Hosho K, Murawaki Y. The influence on liver parenchymal function and complications of radiofrequency ablation or the combination with transcatheter arterial embolization for hepatocellular carcinoma. Hepatol Res 2004; 29: 18-23.

[18] Li JX, Wu H, Huang JW, Zeng Y. The influence on liver function after transcatheter arterial chemoembolization combined with percutaneous radiofrequency ablation in patients with hepatocellular carcinoma. J Formos Med Assoc 2012; 111: 510-515.

[19] Cizginer S, Tatli S, Hurwitz S, Tuncali K, Silverman SG. Biochemical and hematologic changes after percutaneous radiofrequency ablation of liver tumors: experience in 83 procedures. J Vasc Interv Radiol 2011; 22: 471-478.

[20] Liu R, Li K, Luo H, Zhang W, Zhang T, Gao M, Zha W, Cui X, Deng Y. Ultrasound-guided percutaneous microwave ablation for small liver cancers adjacent to large vessels: long-term outcomes and strategies. Oncology 2017; 2: 57-64.

[21] Huang HW, Influence of blood vessel on the thermal lesion formation during radiofrequency ablation for liver tumors. Med Phys 2013; 40: 073303.

[22] Jain P, Tripathi BK, Gupta B, Bhandari B, Jalan D. Evaluation of aspartate aminotransferase-to-platelet ratio index as a non-invasive marker for liver cirrhosis. J Clin Diagn Res 2015; 9: OC22-OC24.

[23] Forestier J, Dumortier J, Guillaud O, Ecochard M, Roman S, Boillot O, Lutringer DM, Scoazec JY, Subtil F, Mion F. Noninvasive diagnosis and prognosis of liver cirrhosis: a comparison of biological scores, elastometry, and metabolic liver function tests. Eur J Gastroenterol Hepatol 2010; 22: 532-540.

[24] Wiesner RH, Edwards EB, Freeman RB, Harper A, Kim RW, Kamath PS, Kremers WK, Lake JR, Howard TK, Merion RM. Model for end-stage liver disease (MELD) and allocation of donor livers. Gastroenterology 2003; 124: 91-96.