Local Anesthesia vs. General Anesthesia for Percutaneous Microwave Ablation in Hepatocellular Carcinoma, an Efficacy, Safety, and Cost Analysis

Jing-Yin Zhan
the Second Xiangya Hospital of Central South University
Zhen-Lei Tang
the Second Xiangya Hospital of Central South University
Hao-Qun Leng (503472@csu.edu.cn)
the Second Xiangya Hospital of Central South University

Research Article

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Abstract

Purpose: To compare the efficacy, safety, and cost between local anesthesia and general anesthesia modality for percutaneous microwave ablation in hepatocellular carcinoma patients who received combination therapy for curative treatment purposes.

Methods: This comparative, retrospective analysis analyzed 175 patients treated for hepatocellular carcinoma (HCC) from July 2015 to September 2020. Patients were divided into two cohorts according to the anesthesia modality applied during the percutaneous microwave ablation (MWA) procedure. To investigate the differences in efficacy between the two groups, overall survival (OS) and local recurrence-free survival (LRFS) were estimated by the Kaplan-Meier method and compared by the log-rank test. Propensity score matching (PSM) was performed using a caliper width of 0.2 between two groups. Cost and safety between the two groups were also compared accordingly.

Results: There was 105 patients with 128 HCC lesions in the local anesthesia (LA) group while 70 patients with 107 lesions in the general anesthesia (GA) group. No significant differences in OS (P=0.798) and LRFS (P=0.406) between the two groups. 51 pairs of patients were matched with 78 lesions in the GA group and 68 lesions in the LA group after PSM. There were no significant differences in the OS (P=0.522) and LRFS (P=0.410) between the two groups as well. Compared to the LA group, there was more MWA procedure time spent, medical resources consumption, and financial stress undertaken in the GA group. However, no statistical differences were observed in post-ablation pain, adverse events, and complications between the two groups.

Conclusion: Due to the higher cost of general anesthesia, local anesthesia may be more adaptive during ablation procedure for HCC patients within Milan criteria.

Background

Liver cancer remains a global health challenge worldwide while hepatocellular carcinoma (HCC) accounts for about 90%. According to several guidelines, percutaneous ablation is recommended as a curative therapy for patients with early-stage HCC who are not candidates for surgical resection and liver transplantation [1–3]. Advantages of percutaneous ablation over surgical resection include less invasive, low morbidity, few complications, outpatient use, and repeatability for recurrence of lesions [4]. Moreover, the ablation scope of HCC can be extended by combining adjunctive methods such as transcatheter arterial chemoembolization (TACE), and the treatment efficacy is verified by some studies [5–7]. Therefore, percutaneous ablation is widely applied in early HCC patients as a curative therapy.

Pain management is still a big concern during ablation procedural. intraoperative and postoperative pain, anxiety, and intraoperative respiratory movement may affect the treatment efficacy and safety of ablation. Nowadays, local anesthesia (LA) combined with intravenous sedation or general anesthesia (GA) is applied most frequently during ablation procedural, but the most appropriate anesthesia method is still a highly debated topic worldwide [8].

Therefore, the purpose of the present study was to investigate the treatment efficacy, safety, and cost between general anesthesia and local anesthesia combined with sedation during ablation procedure for HCC patients who received combination therapy for curative treatment purposes.

Materials And Methods

Study design and population

This retrospective study was approved by the institutional review board of our hospitals and was performed following the Declaration of Helsinki. Due to the retrospective nature of the present study, the requirement for written informed consent was waived by the institutional review boards.

From July 2015 to September 2020, a total of 290 consecutive patients with unresectable HCC who received TACE plus MWA were included. Patients meeting the following criteria were included in this study: (a) diagnosed as HCC by Li-RADS 5 category or biopsy; (b) the absence of macrovascular invasion or distant metastasis; (c) preserved liver function (Child-Pugh A or B); (d) Eastern Cooperative Oncology Group performance status 0. The exclusion criteria included (a) lost follow-up (n = 39); (b) beyond Milan criteria (single lesion within 5cm or no more than three nodules with the largest lesion within 3 cm) (n = 26); (c) infiltrative HCC (n = 18); (d) received other treatment for HCC lesions before TACE plus MWA (n = 32). Finally, 175 patients with 235 HCC lesions were included in the present study. The flowchart of the study population is shown in Fig. 1.

TACE procedure

TACE was performed by several board-certified senior interventional radiologists. The femoral artery was routinely catheterized and digital subtraction angiography (DSA) of the superior mesenteric- and celiac artery using a 5-Fr RH catheter (Terumo Co. Ltd, Tokyo, Japan). After hepatic arteriography, a coaxial microcatheter was placed as super-selectively as possible in the tumor feeders to slowly inject the emulsion of iodized oil (Lipiodol, Guerbet Group, France) and epirubicin/doxorubicin. The Lipiodol-epirubicin/doxorubicin emulsion was created by a mixture of up to 15 mL of Lipiodol and distilled water, dissolving 50 mg to 120 mg of epirubicin or 100 mg of doxorubicin at a ratio of 3:1 or 2:1, respectively. The gelfoam slurry was injected through the microcatheter to embolize the proximal tumor feeders. All the procedures were performed technically successful according to the Society of Interventional Radiology (SIR) guidelines [9].

Anesthesia modality

The pre-anesthesia evaluation was performed according to the American Society of Anesthesiologists (ASA) physical status classification system for patients in the GA group [10]. All the patients were ASA physical status I or II. Sedation, laryngeal mask insertion, monitoring of hemodynamics, and electrocardiogram were performed during general anesthesia. The GA group was given propofol, midazolam, and fentanyl/sufentanil via the veins to complete anesthesia induction and received laryngeal mask placement and mechanical ventilation. All patients lost consciousness during the procedure. Sevoflurane and/or propofol were used intravenously to maintain patients under general anesthesia. All the drug doses used during the ablation procedure in the GA group were commissioned by a certified anesthesiologist. The patient in the GA group recovered from general anesthesia in the post-anesthesia care unit after the MWA procedure finished.

In the group of LA plus intravenous sedation (Hereinafter abbreviated as LA group), about 10 mL of 2% lidocaine was injected subcutaneously at the puncture point. A unit of midazolam and fentanyl, as starting dose of sedation, was intravenously injected to control intraoperative pain and anxiety. During MWA procedural, the sedation dose would increase according to the operation time and patients' pain level. Hemodynamic and electrocardiogram monitoring was performed, and the patient was kept awake and breathed spontaneously intraoperatively.

Percutaneous Microwave ablation procedure

All tumors were percutaneously ablated within 3 days of embolization of the tumor vessels with iodized oil and gelatin sponges, and TACE plus the following MWA were performed in single hospitalization. Percutaneous microwave ablation was performed under microwave ablation (MWA) systems (KY-2000, Kangyou Medical Instrument Co. Ltd., China) by two board-certified senior interventional radiologists (one with more than 15 years of experience in percutaneous ablation while another one with 9 years). Before the insertion of the ablation needle, an unenhanced computed tomography (CT) was carried out and previous imaging data were reviewed, and then the antenna was percutaneously inserted into the lesion under CT guidance. The overlapping ablation technique was performed for tumor lesions larger than 3.0 cm. The MWA was set from 60 W to 140 W, and the ablation time was 3 min to 15 min. If necessary, artificial ascites were created through a fine hollow needle, especially for lesions in subcapsular locations. All the visible HCC lesions were treated during the same ablation procedure by using single ablation modality. The respiratory motion of patients in the GA group was regulated with the help of an anesthesiologist during ablation procedures.

Contrast-enhanced multiphase CT (including arterial, portal, and delayed phases) was performed immediately after ablation for patients with indistinct ablation margin, and immediate complications and technical success were assessed. The technical success of MWA was defined as complete ablation of the tumor with a safety margin of at least 0.5 cm on CT images. For residual viable tumors, repeated ablation procedure was applied till technical success achieved.

Data collection

The demographic, laboratory, and radiological data of patients before TACE plus MWA were collected for each patient, including age (≤ 59 years/>59 years), gender (male/female), Child-Pugh class (A/B), etiology of hepatitis (none/hepatitis B/hepatitis C/alcohol/others), serum alpha-fetoprotein (AFP) level (≤ 400 ng/mL/>400 ng/mL), cirrhosis (presence/absence), number of tumors (single/multiple), tumor size (≤ 3 cm/>3 cm), perivascular (yes/no) and subcapsular (yes/no). Patients were stratified based on the median age (59 years) in the present cohort. Perivascular HCC lesions were defined as lesions adjacent to larger vessels (> 3mm) while subcapsular lesions were located within 1 mm of the liver capsule [11, 12]. MWA procedure-related data, including duration of the MWA procedure, Number of healthcare providers participated, and adverse events (AEs) or complications, were also recorded. The duration of the MWA procedure is defined as the time between the patient entering and leaving the operation room. The post-ablation pain is recorded within 24h after the MWA procedure, and classified as mild pain (5–44 mm), moderate pain (45–74 mm), and severe pain (75–100 mm) according to the VAS criteria [13]. We also recorded the hospital stay and hospitalization costs for every patient.

Definitions and follow up

Local tumor recurrence (LTR) was defined as the appearance of viable tumor foci at the edge of the ablation zones after complete response (CR) at least one contrast-enhanced follow-up imaging. Local recurrence free survival (LRFS) was defined as the interval from ablation to the LTR of the target lesion or the last imaging follow-up (classified as censored data). Overall survival (OS) was the time interval between the first ablation and death from any cause or last follow-up (classified as censored data) (Oct 03, 2021). Ablation related complications were jointly evaluated according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE Version 5.0) [14] and the Society of Interventional Radiology (SIR) classification system [15]. The severity of post-ablation pain is determined according to the distribution of pain Visual Analogue Scale/Score (VAS).

Patients were followed up at 1, 3, 6, 9, and 12 months after TACE plus MWA procedural in the first year and every 6 months in subsequent years. At each follow-up visit, contrast-enhanced Magnetic resonance (MR) of the liver was performed to evaluate LTR. The choice of treatment modality for recurrent HCC was dependent on the site of the tumor, liver function, and the general condition of the patient. The primary endpoint of our study was LRFS for lesions, and the secondary endpoint was OS for patients. The ablation evaluation standards were based on the modified response evaluation criteria in solid tumors (mRECIST) guidelines [16].

Statistical analysis

Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. Continuous variables were compared using the Mann-Whitney U test or t-test accordingly. To diminish potential confounding and selection bias of the two groups, propensity score matching (PSM) methods were applied. PSM is a statistical matching technique that attempts to reduce the bias due to confounding variables that could be found in an estimate of the treatment effect [17]. All the factors which may affect the outcome of ablation procedure were included for propensity score matching. GA and LA groups were matched by using one to one PSM method with a caliper width of 0.2. The LRFS for lesions and OS for patients between two groups were estimated by the Kaplan-Meier method and compared by the log-rank test. Stratification analyses were performed, to compare the LRFS for lesions, in the subgroup of perivascular (yes/no) and subcapsular (yes/no) after PSM. The differences in safety and cost between GA and LA groups were analyzed before and after PSM appropriately. A two-sided P value less than 0.05 indicated statistical significance. Statistical software (SPSS version 24, International Business Machines

Corporation, USA) or R software (version 4.0.2, http://www.R-project.org) were carried out for statistical analysis.

Results

Baseline patient characteristics

175 treatment naïve HCC patients with 235 lesions were enrolled in our study, including 142 males and 33 females, with a mean age of 59.2 ± 11.3 years, ranging from 27 to 83 years. There were 105 patients with hepatitis B, 20 patients with hepatitis C, 15 patients with alcoholic hepatitis, 18 patients with other etiologies of hepatitis, and 17 patients without basic hepatitis. Patients diagnosed with HCC were based on pathology (n = 21) or the 2018 version of the LI-RADS criteria (n = 154). There were 148 patients with Child-Pugh A and 27 patients with Child-Pugh B. In the entire study population, there were 70 patients with 107 HCC lesions in the GA group, and the LA group included 105 patients with 128 lesions. After one-to-one PSM, there were 52 pairs of patients matched, with 77 lesions in the GA group and 67 lesions in the LA group. The detailed baseline characteristics between GA and LA groups before and after PSM were illustrated in Table 1.

Table 1
Baseline characteristics of GA group and LA group before PSM and after PSM

Characteristics	Before PSM			After PSM		
	GA group (n = 70)	LA group (n = 105)	P	GA group (n = 52)	LA group (n = 52)	P
Gender	62	80	0.040	45	43	0.587
Male	8	25	0.267	7	9	0.239
Female						
Age						
≤ 59	38	48		29	23	
> 59	32	57		23	29	
Number of tumors			< 0.001			0.292
single	37	86		33	38	
multiple	33	19		19	14	
Tumor size			0.267			0.534
≤ 3 cm	43	73		33	36	
> 3 cm	27	32		19	16	
Perivascular			0.497			0.695
Yes	33	55		26	28	
No	37	50		26	24	
Subcapsular			0.014			0.163
Yes	49	54		34	27	
No	21	51		18	25	
Child-Pugh score			0.698			0.604
A	58	90		42	44	
B	12	15		10	8	
Etiologies of hepatitis			0.011			0.441

Note: In patients with multiple lesions, the characteristics of the largest lesion were used for analysis

Abbreviations: GA, General anesthesia; LA, Local anesthesia; PSM, Propensity score matching; AFP, Alpha fetoprotein

Characteristics	Before PSM			After PSM		
	GA group (n = 70)	LA group (n = 105)	P	GA group (n = 52)	LA group (n = 52)	P
None	3	14		3	4	
HBV	53	52		36	31	
HCV	4	16		3	9	
Alcohol	4	11		4	3	
Others	6	12		6	5	
Cirrhosis			< 0.001			0.365
Yes	43	93		37	41	
No	27	12		15	11	
AFP			0.584			1.000
≤ 400 ng/mL	62	90		45	45	
> 400 ng/mL	8	15		7	7	
Note: In patients with multiple lesions, the characteristics of the largest lesion were used for analysis						
Abbreviations: GA, General anesthesia; LA, Local anesthesia; PSM, Propensity score matching; AFP, Alpha fetoprotein						

Comparison of LRFS and OS between GA and LA group before and after PSM

There were 70 patients with 107 HCC lesions in the GA group, while 105 patients with 128 lesions in the LA group before PSM. There was no difference in the OS between the two groups, with the same 1-year survival rate (92% vs 94%, P = 0.798). No significant difference was observed in the LRFS of the treated lesion between the GA and LA groups, with P = 0.406. After a one-to-one PSM analysis, there were 52 pairs of matched patients with 77 lesions in the GA group and 67 lesions in the LA group. No significant difference was observed in the OS (P = 0.861) and LRFS (P = 0.637) between the two groups after PSM analysis. Figures 2 and 3 demonstrated the survival curve of OS and LRFS between the GA and LA groups before and after PSM.

Subgroup analysis

After a one-to-one PSM analysis, 77 lesions in the GA group and 67 lesions in the LA group were matched. In the subgroup of perivascular lesions, there were no significant differences in LRFS between the GA and LA groups (P = 0.727) (Fig. 4A). meanwhile, no significant difference was observed in LRFS of non-perivascular lesions between the GA and LA groups, with P = 0.918 (Fig. 4B). In the subgroup of lesions with and without subcapsular location, both lesions with subcapsular location (P = 0.879) (Fig. 4C) and without subcapsular location (P = 0.679) (Fig. 4D) demonstrated no differences in LRFS between GA and LA group.

Cost analysis

Costs in both MWA procedure time, medical resources consumption, and financial stress undertaken by each patient were recorded accordingly. The MWA procedure time consuming for the GA group (133.8 ± 26.0 mins) was significantly longer than the LA group (100.3 ± 18.4 mins) (P = 0.017). Furthermore, there were more healthcare providers participated in the MWA procedure for the GA group (5.2 ± 0.9) than the LA group (3.0 ± 0.7) (P = 0.003). All the hospitalization costs were figured out in the discharge settlement, patients cost¥45.0 ± 4.3k in the GA group while¥38.8 ± 1.3k in the LA group ($p < 0.001$). As for the hospital stays, there was no statistical difference between the GA group (5.2 ± 1.0 days) and the LA group (5.0 ± 1.2 days) ($p = 0.390$). The cost analysis between GA and LA groups showed a similar outcome after PSM. The detailed category and information are illustrated in Tables 2 and 3.

Table 2
Cost analysis between GA and LA group before PSM

Category	GA group (n = 70)	LA group (n = 105)	*p*
MWA procedure time (min)	133.8 ± 26.0	100.3 ± 18.4	0.017
Healthcare providers participated	5.2 ± 0.9	3.0 ± 0.7	0.003
Hospitalization costs (¥; K)	45.0 ± 4.3	38.8 ± 1.3	< 0.001
Hospital stays (day)	5.2 ± 1.0	5.0 ± 1.2	0.390
Abbreviations: GA, General anesthesia; LA, Local anesthesia; PSM, Propensity score matching; MWA, Microwave Ablation			

Table 3
Cost analysis between GA and LA group after PSM

Category	GA group (n = 52)	LA group (n = 52)	*p*
MWA procedure time (min)	130.58 ± 25.82	97.89 ± 18.42	< 0.001
Healthcare providers participated	5.23 ± 0.85	2.92 ± 0.71	< 0.001
Hospitalization costs (¥; K)	45.34 ± 4.17	38.75 ± 1.28	< 0.001
Hospital stays (day)	5.19 ± 1.03	5.25 ± 1.25	0.789
Abbreviations: GA, General anesthesia; LA, Local anesthesia; PSM, Propensity score matching; MWA, Microwave Ablation			

Post-ablation pain, AEs and Complication

The post-ablation pain is recorded within 24h after the procedure and classified as mild, moderate, and severe pain. In the GA group, there are 41, 21 and 8 patients with mild, moderate, and severe pain respectively while 52, 37, and 16 patients in the LA group ($p = 0.487$). Fever (with/without treatment) was the most common AEs and no significant statistical differences were observed in all the occurred AEs between GA and LA groups. The incidences of Hemolytic uremic syndrome, pleural effusion, liver abscess, asymptomatic perihepatic fluid, and subcapsular hepatic hemorrhage in the GA group were (4%), (6%), (3%), (7%) and (3%), respectively. In the LA group, the complication rates were (5%), (6%), (4%), (7%), and (3%), respectively. Similar results were observed between GA and LA groups after PSM. All the ablation related AEs and complications accepted heteropathy accordingly, and no life-threatening complications during treatment occurred. The detailed category and information are summarized in Tables 4 and 5.

Table 4
Post-ablation pain, adverse events and complications analysis between GA and LA group before PSM

Category	**GA group (n = 70)**		**LA group (n = 105)**		***p***
	Grades	**Number (%)**	**Grades**	**Number (%)**	
Post-ablation pain					0.487*
	Mild	41 (59)	Mild	52 (50)	
	Moderate	21 (30)	Moderate	37 (35)	
	Severe	8 (11)	Severe	16 (15)	
Adverse events					
Fever, maximum 38°C, no treatment	I	7 (10)	I	11 (10)	0.919*
Fever, > 38°C, treatment	II	52 (74)	II	75 (71)	0.678*
Nausea or vomiting	II	13 (19)	II	18 (17)	0.808*
Mild liver dysfunction, requiring conservative treatment	II	29 (41)	II	41 (39)	0.753*
Complications					
Hemolytic uremic syndrome	III	3 (4)	III	5 (5)	0.595§
Pleural effusion	III	4 (6)	III	6 (6)	0.622§
Liver abscess	III	2 (3)	III	4 (4)	0.544§
Asymptomatic perihepatic fluid	IV	5 (7)	IV	7 (7)	0.703*
Subcapsular liver hemorrhage	IV	2 (3)	IV	3 (3)	0.666§

Visual Analog Scale (VAS) for Post-ablation pain.

National Cancer Institute Common Terminology Criteria for Adverse Event (CTCAE version 4.03)

Society of Interventional Radiology (SIR) classification system for Complications.

Data are numbers of events. Data in parentheses are percentages

Abbreviations: GA, General anesthesia; LA, Local anesthesia; PSM, Propensity score matching; MWA, Microwave Ablation

*Pearson $\chi 2$ test was used. §Fisher exact test was used.

Table 5
Post-ablation pain, adverse events and complications analysis between GA and LA group after PSM

Category	GA group (n = 52)		LA group (n = 52)		*p*
	Grades	**Number (%)**	**Grades**	**Number (%)**	
Post-ablation pain					0.371*
	Mild	29 (56)	Mild	22 (42)	
	Moderate	17 (33)	Moderate	21 (40)	
	Severe	6 (11)	Severe	9 (17)	
Adverse events					
Fever, maximum 38°C, no treatment	I	5 (10)	I	6 (12)	0.750*
Fever, > 38°C, treatment	II	38 (73)	II	39 (75)	0.823*
Nausea or vomiting	II	11 (21)	II	10 (19)	0.807*
Mild liver dysfunction, requiring conservative treatment	II	21 (40)	II	21 (40)	1.000*
Complications					
Hemolytic uremic syndrome	III	3 (6)	III	1 (2)	0.308§
Pleural effusion	III	4 (8)	III	5 (10)	0.727§
Liver abscess	III	1 (2)	III	3 (6)	0.308§
Asymptomatic perihepatic fluid	IV	3 (6)	IV	4 (8)	0.696§
Subcapsular liver hemorrhage	IV	1 (2)	IV	0 (0)	0.315§

Visual Analog Scale (VAS) for Post-ablation pain.

National Cancer Institute Common Terminology Criteria for Adverse Event (CTCAE version 4.03)

Society of Interventional Radiology (SIR) classification system for Complications.

Data are numbers of events. Data in parentheses are percentages

Abbreviations: GA, General anesthesia; LA, Local anesthesia; PSM, Propensity score matching; MWA, Microwave Ablation

*Pearson χ2 test was used. §Fisher exact test was used.

Discussion

CT-guided percutaneous thermal ablation is a minimally invasive therapy to treat focal tumors by inducing irreversible cellular injury through the application of thermal energy, and MWA is one of the mainstream ablation methods. As a curative therapy for early-stage HCC, the primary purpose of ablation is to completely eradicate all viable malignant cells within the target HCC lesions [18]. The treatment efficacy of ablation for relatively small HCC lesions is comparable to radical surgical resection [1, 2, 19]. The therapeutic scope of ablation can be extended by combining adjunctive methods such as TACE. TACE performed before thermal ablation could diminish the blood flow into the HCC lesions and lead to a larger ablation zone during the ablation procedure.

In our study, no significant difference was observed in LRFS and OS rate between GA and LA groups both before and after PSM. Local tumor recurrence could hamper the treatment efficacy of MWA greatly. Liver transplantation is by far the most effective therapy for liver cancer, patient selection has resulted in remarkable 10-year post-liver transplantation survival rates for HCC patients within Milan criteria [3]. However, many HCC patients within Milan criteria dropped out while waiting for the transplanted liver source causing the progression disease. To receive increased allocation priority, HCC patients who are listed for liver transplantation are often treated while on the waiting list with loco-regional therapy (LRT) such as ablation and/or TACE [20]. Moreover, complete response (CR) to LRT demonstrated in the first follow-up imaging study were more likely to undergo liver transplantation. All the patients enrolled in our study were within Milan criteria and all the patients achieved technical success and CR on the first follow-up enhanced MR. Our results demonstrated no significant difference in local tumor progression between GA and LA groups. This result indicated that both local anesthesia plus intraoperative sedation and general anesthesia are effective anesthesia modalities for CT-guided ablation in HCC patients within Milan criteria. However, the liver transplantation rate after combined therapy failed to record causing a short follow-up period and considerable censored data. Whether the anesthesia modality in the MWA procedure will affect the successful rate and therapeutic efficacy of following liver transplantation still need further investigation.

Local anesthesia combined with intravenous sedation is still the mainstay anesthesia modality for MWA, while general anesthesia also applied in some interventional therapy centers. Few studies focused on the comparison among different anesthesia methods in ablation procedure for hepatocellular carcinoma. The study of Lai et al. [21] suggested that treatment of small HCC with RFA under GA is associated with reducing the risk of cancer recurrence. Another study conducted by Wang et al. [22] demonstrated that applying GA in the thermal ablation of HCC patients could significantly improve the survival time of patients compared to LA. Some authors also argued that patients under LA suffered from pain and stress during the ablation procedure, thus leading to insufficient ablation zone [23]. On the other hand, the study by Li et al. revealed that different anesthesia methods have no significant effect on treatment-related complications and LTP in HCC patients treated by MR-guided MWA [24]. Whether the anesthesia modality would affect the therapeutic of percutaneous ablation in HCC patients is still in debate. In our study, no significant differences were observed in the LRFS and OS rate between the two different anesthesia modalities. This outcome is mainly due to the following reasons. First of all, most patients accepted local anesthesia plus sedation during the ablation procedure in our study could control their respiratory movement during needle insertion. To achieve a good therapeutic response to MWA, the precise insertion and placement of the ablation antenna are crucial. For patients who were unable to control their respiratory movement, multiple punctures were performed until the ablation antenna was inserted into the desired position. Secondly, TACE performed before MWA served as an adjunctive method, and the lipiodol deposited in the HCC lesions is a conspicuous marker during the MWA procedure. According to the lipiodol label, ablation antenna could be inserted through the center of HCC lesions in most cases regardless of the anesthesia modality. Moreover, TACE before MWA could diminish the blood flow into the lesions and enhance the power of thermal ablation, thus improving the treatment efficacy of the following MWA [25].

In the stratification analysis in LRFS of lesions, no significant differences were observed between different anesthesia modalities. HCC lesions in perivascular and/or subcapsular location were deemed as unfavorable location. Heat sinks effect were common for perivascular lesions, large vessels with higher flow could draw away heat from the ablative area. Theoretically, lesions in the perivascular location might be more beneficial from general anesthesia than local anesthesia during the ablation procedure. The possible reason for this discrepancy may be that HCC lesions enrolled in our study were all treated by MWA, and the MWA procedure could create high-temperature heating and lack of heat sink effects [26, 27]. Moreover, lipiodol deposited in the HCC lesions, as aforementioned, could diminish the hepatic artery inflow and reduce the “heat-sink” effect, thus enhancing the efficacy of subsequent ablation [25, 28].

Subcapsular location is challenging for percutaneous ablation due to the difficulty of accurate insertion of the ablation needle and obtaining enough ablative margin along the hepatic capsule. On the other hand, underlying thermal injury of adjacent structures for subcapsular lesions associated with a higher risk of major complications. No significant difference in LRFS between GA and LA groups for subcapsular lesions might attribute to the following reasons. In our study, artificial ascites was used, regardless of the anesthesia modality, to create hydrodissection for subcapsular lesions as appropriate [29]. Consequently, treatment related complications were reduced while ablation efficacy improved. On the other hand, deposited lipiodol in HCC lesions enhanced the visibility of subcapsular lesions thus improving the accuracy of ablation antenna insertion [28].

There was no significant difference in the occurrence of treatment related AEs and complications before and after PSM. This result demonstrated that both general and local anesthesia were safe and feasible anesthesia modalities during the MWA procedure. As for cost analysis, the GA group presented a longer MWA procedure time, more healthcare providers participated, and more hospitalization costs. It is worth mentioning that both GA and LA groups have comparable hospital stays, and this may be attributed to no significant difference in the occurrence of treatment related AEs and complications. In this regard, general anesthesia is more costly compared to local anesthesia but showed a comparable treatment efficacy and safety.

There are several limitations in the present study. First, this was a single-center and retrospective study with an inevitable bias. Although propensity score-matching (PSM) was applied to diminish potential confounding and selection bias, there were still some heterogeneous between the two anesthesia groups. Second, the detail of the MWA procedure, such as the power and ablation time, were not recorded specifically. This drawback might hamper the rigor of the results in our study, as the parameters of the MWA procedure were critical for the therapeutic efficacy. Third, TACE performed before MWA may increase the rate of AEs and complications related to the MWA procedure. Last but not least, the limited follow-up period of the study may have impeded the thorough survival assessment of the patients. The long-term therapeutic outcomes of the two anesthesia groups during the MWA procedure need further investigation.

Overall, our retrospective study demonstrated no significant differences in the therapeutic outcomes between general anesthesia and local anesthesia plus sedation. Moreover, both the two-anesthesia modalities, during the MWA procedure, were safe and effective for HCC patients within Milan criteria. However, the cost in both procedure time, healthcare providers participated and hospitalization costs of general anesthesia was higher than local anesthesia. Thus, local anesthesia plus sedation may be more adaptive to CT-guided MWA in HCC patients within Milan criteria who received combination therapy for curative purpose.

Abbreviation

Hepatocellular carcinoma (HCC); Microwave ablation (MWA); Transarterial chemoembolization (TACE); Local anesthesia (LA); General anesthesia (GA); Digital subtraction angiography (DSA); Society of Interventional Radiology (SIR); Radiofrequency ablation (RFA); Computed tomography (CT); Magnetic resonance (MR); Local tumor recurrence (LTR); Complete response (CR); Local recurrence-free survival (LRFS); Overall survival (OS); Visual Analogue Scale/Score (VAS); Adverse events (AEs); Propensity score-matching (PSM)

Declarations

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Ethics approval: This retrospective study was approved by the Institutional Ethics Committee of the Second Xiangya Hospital of Central South University, and in accordance with the Declaration of Helsinki.

Consent to participate: Written informed consent was waived by the Institutional Ethics Committee due to the retrospective nature of the present study.

Consent for publication: Not Applicable.

Availability of data and material: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability: Not Applicable

Authors' contributions: JY Zhan, ZL Tang, and HQ Leng analyze and interpret the patients' data and review the patients' images. JY Zhan and ZL Tang collect the data. HQ Leng and JY Zhan revise the manuscript. JY Zhan and HQ Leng are major contributors to writing the manuscript. HQ Leng provides the concept and is a major contributor to the manuscript editing. All authors read and approve the final manuscript.

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Figures

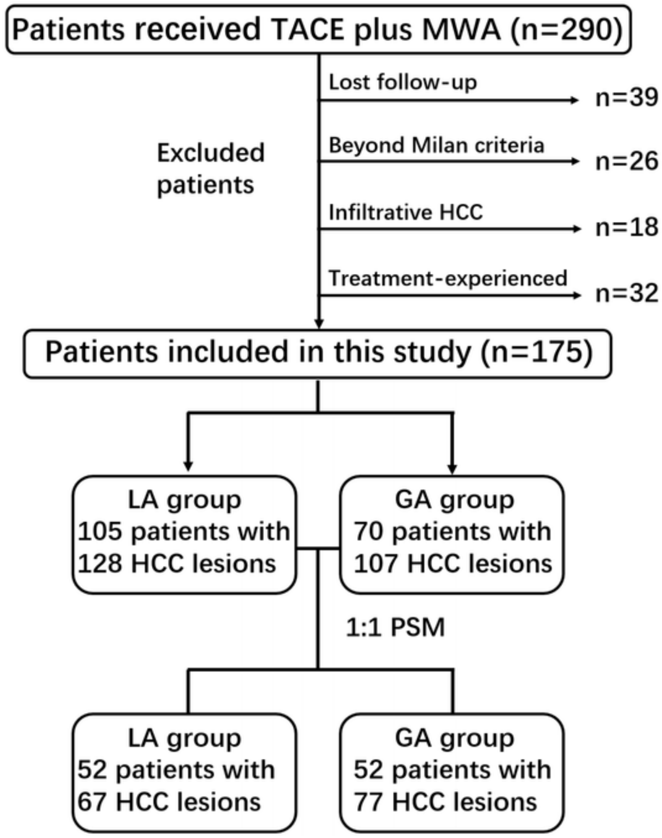

Figure 1

The flowchart of the study population.

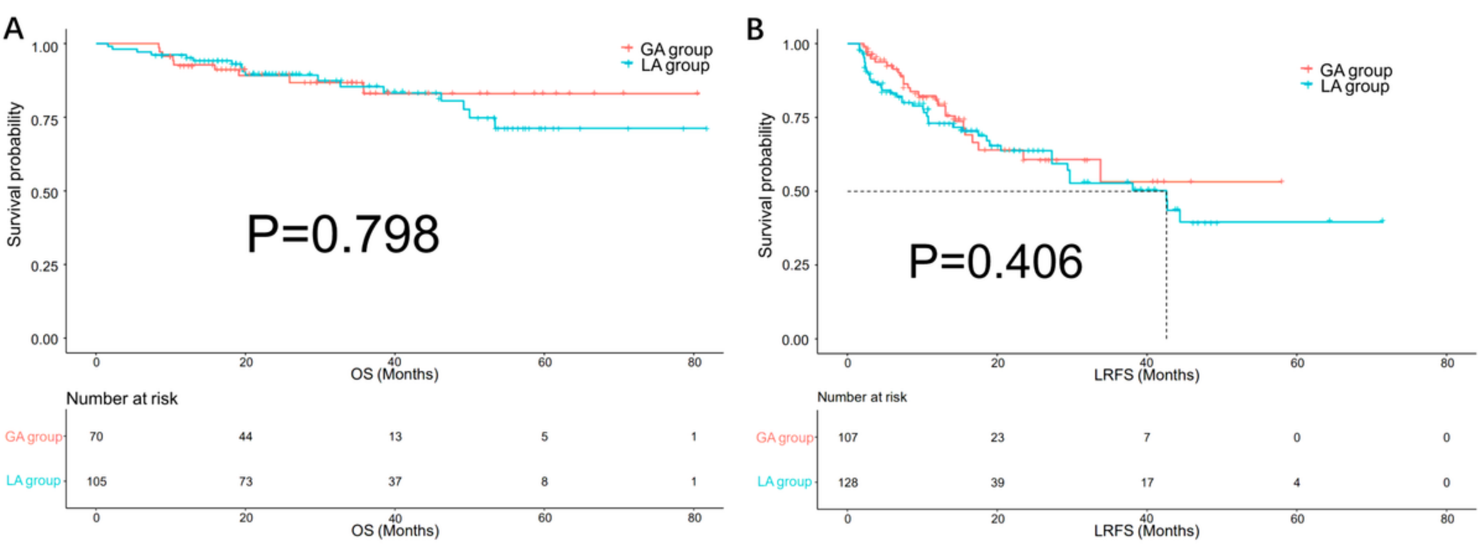

Figure 2

Kaplan-Meier overall survival (OS) curves (A) of patients and local recurrence-free survival (LRFS) curves (B) of lesions in the GA group and LA group before propensity score matching (PSM).

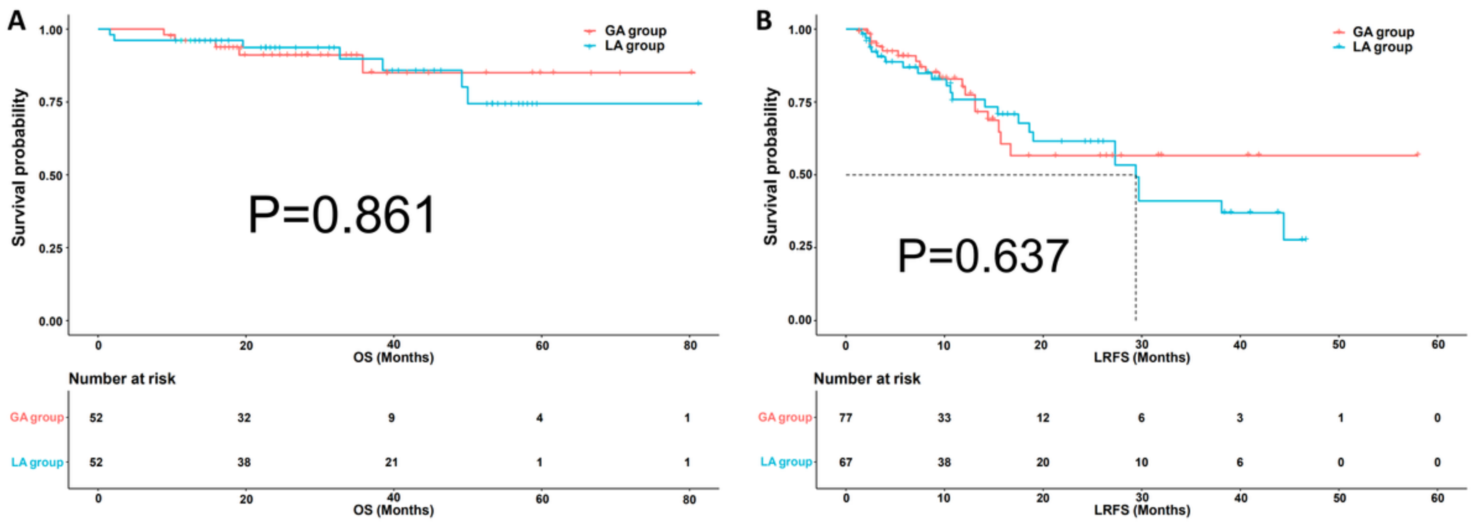

Figure 3

Kaplan-Meier overall survival (OS) curves (A) of patients and local recurrence-free survival (LRFS) curves (B) of lesions in the GA group and LA group after propensity score matching (PSM).

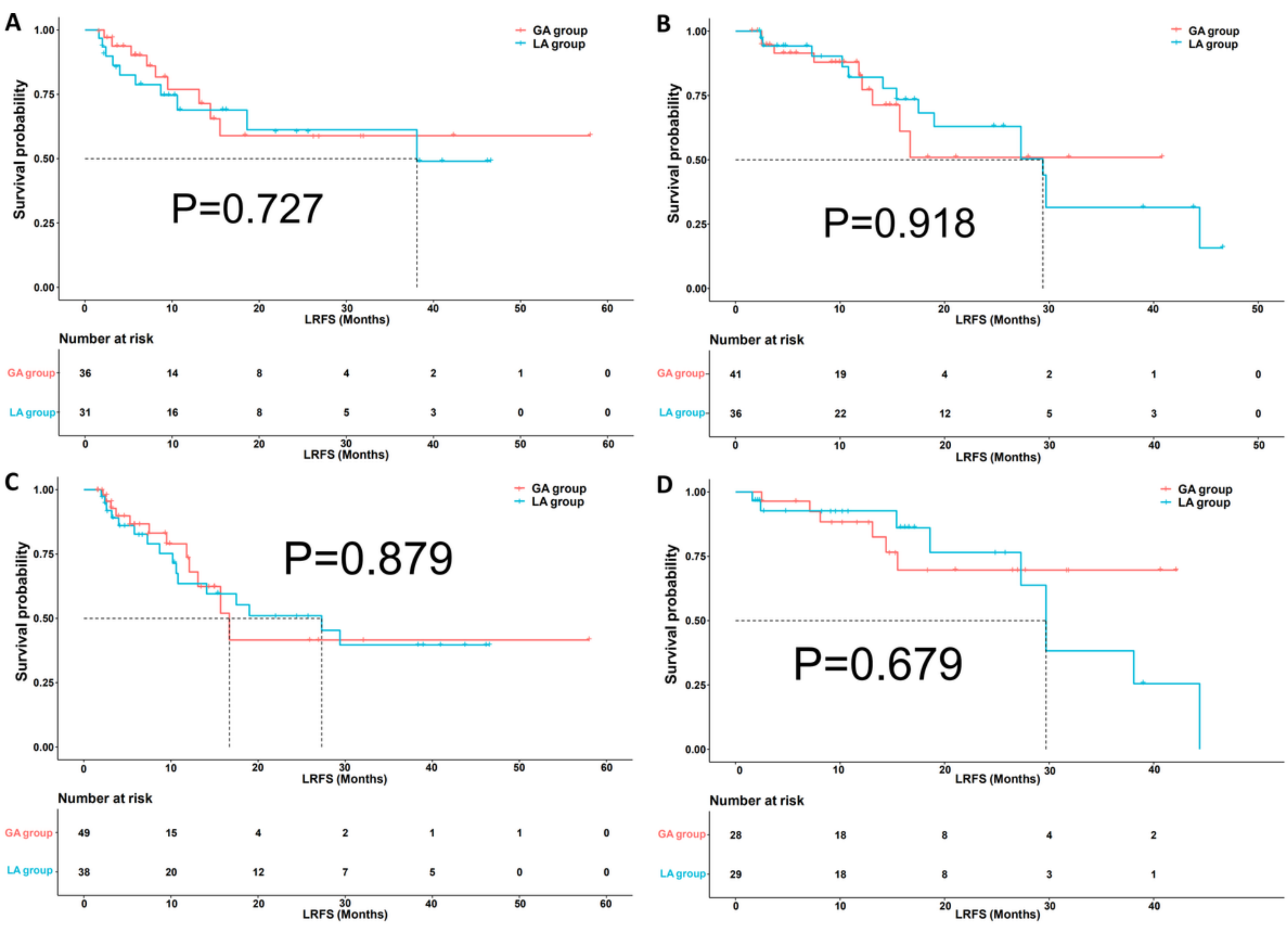

Figure 4

Kaplan-Meier local recurrence-free survival (LRFS) curves of lesions in perivascular (A), non- perivascular (B), subcapsular (C), and non-subcapsular (D) locations between GA group and LA group after propensity score matching (PSM).