**Title Page**

***Title:* Microwave Ablation Provides Better Survival than Liver Resection for Hepatocellular Carcinoma in Patients with Borderline Liver Function: Application of ALBI score to Patient Selection**

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**Abstract**

**Background**

Studies comparing microwave ablation (MWA) and liver resection are lacking. This study evaluates the survival of patients with hepatocellular carcinoma (HCC) treated with liver resection or MWA and the role of Albumin-Bilirubin (ALBI) score in patient selection for treatments.

**Methods**

This is a retrospective analysis of patients who received curative liver resection or MWA for HCC. Propensity score matching was used at a 1:1 ratio. The value of ALBI grade for patient selection was evaluated. Overall and disease-free survival were compared between two groups.

**Results**

Of the 442 patients who underwent MWA or liver resection for HCC during the study period, 63 patients received MWA and 379 patients received liver resection. Propensity scoring matching analysis resulted in 63 matched pairs for further analysis. Subgroup analysis according to the ALBI grade was performed. Liver resection offered better overall and disease-free survivals in patients with ALBI grade 1. MWA provided a significantly better overall survival (p=0.025) and a trend towards better disease-free survival (p=0.39) in patients with ALBI grade 2 or 3.

**Conclusions**

Liver resection offered superior disease-free survival to MWA in patients with HCC. The ALBI grade could identify patients with worse liver function who might gain survival advantage from MWA.

**Keywords**

Hepatectomy; liver resection; local ablation; microwave ablation; hepatocellular carcinoma; Albumin-bilirubin score

**Introduction**

To improve the prognosis of patients with early HCC, it is important to identify those with liver dysfunction in whom the risk of liver resection will outweigh any survival benefit it provides as well as the best ablative method. The degree of underlying liver function is the key in treatment selection. The general consensus is that liver resection should be the treatment of choice in patients with good liver function while local ablation should be considered in patients with poor liver function. However, in reality, there exists a group of patients with apparently good liver function that harbor significant liver cirrhosis which is not easily picked up or detected by the current assessment or scoring systems. Child-Pugh classification is the most widely used scoring systems to define liver dysfunction. Most of patients who receive liver resection are Child’s A. Nevertheless, even in this group of patients liver resection is still potentially life-threatening due to complications and the overall survival is limited. The Albumin-Bilirubin (ALBI) grade has recently been advocated as a valid and objective measure of liver dysfunction. 1 Recent papers have demonstrated that liver function, as classified by ALBI grade, has a major impact on long-term survival after curative treatment for HCC. 2 It also provides more information when incorporated into different staging systems. 3-5 It may, therefore, have a potential role in the selection of patients for local ablation vs liver resection.

Radiofrequency ablation (RFA) and microwave ablation (MWA) are the two most commonly used local ablative methods for HCC. Both are regarded as acceptable curative options for early stage HCC in international guidelines. 6-8 Microwave ablation (MWA) has gained popularity in recent years because of the tremendous progress in the technology of microwave. 9-13 Theoretically, MWA may perform better than RFA as the transmission of microwaves in living tissue is not limited by tissue desiccation and charring. Retrospective studies and meta-analyses have shown MWA is at least as effective as, if not superior to, radiofrequency ablation in treating HCC. 14, 15

Nevertheless, whether MWA can provide similar survival to liver resection and which group of patients can benefit more from MWA remain unknown. The objective of this study is to evaluate the survival of patients treated with liver resection and MWA and to evaluate if the newly developed ALBI grade can help in patient selection for liver resection or MWA.

**Methods**

*Patients*

This is a retrospective review of patients who received potentially curative treatment (liver resection or MWA) for HCC between March 2009 and December 2015 at the Prince of Wales Hospital, Hong Kong. Baseline clinical and laboratory parameters were retrieved from a prospectively collected database. All parameters investigated were measured within the week before treatment. To correct the difference in clinicopathological factors between the two groups, propensity score matching was used at a 1:1 ratio. The following factors were used for propensity matching: sex, age, comorbidities, hepatitis status, serum alpha-fetoprotein (AFP), bilirubin, albumin level, platelet count, INR, tumour size and number.

The ALBI grade was evaluated for its ability to impact on patient selection. Overall and disease-free survivals were compared between the two groups. The ALBI score was computed by the formula, −0.085×(albumin g/l) + 0.66×log(bilirubin µmol/l). Patients were stratified into 3 groups according to previously described cut-offs resulting in 3 grades: ALBI grade 1 (≤−2.60), grade 2 (>−2.60 to −1.39) and grade 3 (>−1.39).10 Portal hypertension was defined according to AASLD/EASL guidelines as the presence of esophageal varices or thrombocytopenia (platelet count <100×109/l) associated with splenomegaly.4, 5 All blood tests, except viral serology, were taken within 1 week before treatment.

*Treatment procedures*

Decision on whether to perform liver resection or local ablation depended on the general condition of the patients, the distribution of the tumour and the liver function at the time of diagnosis. The usual indication for resection was a subcapsular, solitary or oligonodular tumor, in the presence of a sufficient future liver remnant. MWA was generally selected in small and/or deep-seated intra-parenchymal tumour, especially if percutaneous approach was feasible.

**Liver resection**

Liver resection was performed as described previously. 16, 17 Liver parenchymal transection was performed with CUSA (cavitron ultrasonic surgical aspirator) and TissueLink (a radiofrequency saline-linked dissecting sealer). Vascular staplers were used to divide major vascular pedicles. Fibrin glue spray was applied to the parenchymal cut surface of the liver before closure of the abdomen.

**Microwave Ablation**

Microwave ablation (MWA) was performed as in previous reports.9, 12 In short, it was carried out in the operation theatre under general anaesthesia via a laparoscopic or an open approach or percutaneous approach under local anaesthesia in the department of interventional radiology according to the tumours’ location. In the open approach, this was carried out via a right subcostal incision with possible upper midline extension when necessary. After diagnostic laparoscopy in the laparoscopic approach and exploratory laparotomy in the open approach to exclude extra-hepatic disease, operative ultrasound (Aloka, Tokyo, Japan) was performed to exclude preoperatively undetected lesions, to guide insertion of the microwave applicator and to monitor the ablation process. Surrounding organs were cooled by constant irrigation of ice-cold saline to prevent thermal injury. The ablation was carried out according to the standard protocol with the aim to create a 1cm ablation margin around the tumor. The insertion track was burnt after ablation in order to prevent bleeding and tumor seeding.

*Follow-up*

Patients in both arms were followed up by the same team. They were seen every 3 months in the first year, every 4 months in the second year and then 6-monthly thereafter. Chest X-rays, liver function test and serum AFP will be checked during each follow-up. Ultrasound or CT abdomen will be performed every 3 months in the first year postoperatively and every 4 months in the second year. Thereafter, transabdominal imaging will be performed every 6 months. For patients underwent microwave ablation, an additional CT abdomen was performed 1 month after ablation to check the completeness of ablation. Diagnosis of recurrent disease was made if typical imaging findings were noted on a CT or MRI scan. Once recurrence was diagnosed, the management of recurrence depended on the distribution of recurrence and the liver function at the time of recurrence. Cases were reviewed in a multidisciplinary clinic with liver surgeons, interventional radiologists and oncologists for consideration for subsequent therapies. The duration of follow-up was measured from the date of operation to the date of the last follow-up before we analyzed the data or the date of death.

*Outcome Measures*

Overall survival is the primary outcome of this study. Secondary outcomes include disease-free survival, surgical morbidities and mortalities. Overall survival was measured from the time of liver resection or MWA to the time of death or last follow-up if death had not occurred. Disease-free survival was measured from the time of liver resection or MWA to the time of radiological evidence of tumour relapse.

*Statistical analyses*

Continuous variables were expressed in mean ± standard deviation (SD) or median with interquartile range (IQR). Comparison between groups was analyzed by chi-square test or Fisher’s exact test for categorical variables, and Student’s t test or Mann-Whitney test for continuous variables, as appropriate. Correlation was evaluated by the Spearman correlation test. The Kaplan-Meier method was used to estimate the survival rates for different groups. The equivalences of the survival curves were tested by log-rank statistics. Propensity score matching analysis in a 1:1 ratio was employed to minimize the confounding prognostic factors affecting the effectiveness of liver resection and MWA. All statistical analyses were performed using SPSS 15.0 software (SPSS, Chicago, IL, USA). A 2-tailed *P*-value <0.05 was regarded as statistically significant.

**Results**

**(I) Propensity score matching of patients underwent microwave ablation or liver resection**

Of the 442 patients, 63 patients received MWA and 379 patients received liver resection.

Propensity score matching analysis was used to minimize bias and confounding factors in patient selection and generated 63 matched pairs of patients for comparison of efficacy between MWA and liver resection. Baseline characteristics of these patients were well matched (Table1). There were no statistical significant differences on the overall survival rates for patients treated with MWA and liver resection. The 1-, 3- and 5- year overall survival for MWA group vs liver resection group were 98.4% vs 95.2%, 72.3% vs 82.6% and 61.3% vs 79.6% respectively. (p = 0.186) While 41 and 18 patients developed intra-hepatic recurrence in MWA and liver resection group respectively (p<0.001), 9 patients in the MWA group and 2 patients in the liver resection group developed local ablation site or resection site recurrence. (p=0.027) Re-hepatectomy, repeated local ablation by RFA or MWA and transarterial chemoembolization (TACE) were the major treatments for intrahepatic recurrence in this cohort. There was no significant difference in the proportion of re-treated patients in the ablation vs the resection group (97.6% vs. 94.4%, p=0.521). Among 41 patients who developed intrahepatic recurrences in MWA group, 14 patients (34.1%) and 26 patients (63.4%) were treated by repeated local ablation and TACE respectively. Among 18 patients who developed intra-hepatic recurrences in liver resection group, 3 (16.7%), 8 (44.4%) and 6 (33.3%) patients were treated by re-hepatectomy, repeated local ablation and TACE respectively. Only one patient in each group received conservative treatment for recurrence. Liver resection offered superior disease-free survival to MWA. The 1-, 3- and 5- year disease-free survival for MWA group vs liver resection group were 62.5% vs 75.6%, 30.6% vs 65.5% and 17.5% vs 57.5% respectively. (p<0.001) (Figure 1)

***(i) Subgroup analysis on patients with ALBI 1***

The ALBI grade was evaluated for its ability of patient selection. Among 74 patients with ALBI 1, 33 of them received MWA and 41 of them received liver resection. The baseline clinicopathological demographics were comparable between two groups. (Table 2) For patients with good background liver function, i.e. ALBI grade 1, liver resection provided better overall and disease-free survivals than MWA. The 1-year, 3-year, 5-year overall survival for patients with ALBI 1 received MWA and liver resection were 100%, 62.8%, 52.2% and 100%, 96.3%, 96.3% respectively (p<0.001). MWA group was associated with significantly more intrahepatic recurrence (69.7% vs 17.1%, p<0.001). While none of the patients in the liver resection group had local recurrence, 6 (18.2%) in the MWA group developed local intrahepatic recurrence (p=0.006). There was no significant difference in proportion of patients who received retreatment for intrahepatic recurrence between two groups (95.7% vs 100%, p>0.99). The 1-year, 3-year, 5-year disease-free survival for patients with ALBI 1 received MWA and liver resection were 55.6%, 25.5%, 15.3% and 92.6%, 83.2%, 71.5% respectively (p<0.001).

***(ii) Subgroup analysis on patients with ALBI 2/3***

Among 52 patients with ALBI 2/3, 30 of them received MWA and 22 of them received liver resection. Baseline demographics were similar between two groups apart from a lower platelet count in the MWA group. There was no significant difference in the intrahepatic recurrence rate (60.0% vs 50.0%, p=0.473). Three and two patients developed local ablation or resection site recurrence in MWA and liver resection group respectively. (p >0.999). Proportion of patients who received re-treatment for intra-hepatic recurrence were similar between the two groups (100.0% vs 90.9%, p=0.379). For patients with suboptimal liver function, i.e. ALBI grade 2/3, MWA provided a significantly better overall survival (p=0.025) and a trend towards better disease-free survival (p=0.39) compared to liver resection. (Table 3) The 1-year, 3-year, 5-year overall survival for patients with ALBI 2/3 who received MWA and liver resection were 96.7%, 83.4%, 71.5% and 85.9%, 54.9%, 43.9% respectively (p=0.025). Liver resection in patients with ALBI grade 2/3 was associated with a significantly higher complication rate (6.7% vs 50%, p < 0.001), more intra-operative blood loss (836.1 ml vs 30.8 ml, p = 0.002) and a trend towards more blood transfusion (9.1% vs 0%, p=0.174).

**(II) Propensity score matching of patients with Child’s A, ALBI 2 who underwent microwave ablation or liver resection**

Among the 442 patients who underwent MWA or liver resection in the study period, 105 patients had Child’s A cirrhosis and ALBI grade 2. Propensity score matching analysis was repeated this subgroup of patients and resulted in 27 matched-pair of patients for further analysis. Both groups were comparable in terms of age, sex, tumour size, tumour multiplicity and MELD score. (Table 4) Liver resection was again associated with significantly higher complication rate (40.7% vs 7.4%, p = 0.004), more intra-operative blood loss (530.3 ml vs 31.3 ml, p < 0.001). (Table 5) There was no significant difference in intrahepatic recurrence rate between the two groups (55.6% vs 48.1%, p=0.586). Two patients in the MWA group developed local recurrence while none of the patients in the liver resection group developed local recurrence. (p=0.491) While all patients with intrahepatic recurrence were treated in MWA group, only 9 patients (69.2%) of patients in the liver resection group received treatment for intrahepatic recurrence (p=0.035). MWA was associated with a significantly better overall survival (p=0.043) than liver resection. (Figure 2)

**Discussion**

Background liver function is a key element determining the short and long term outcome of early HCC and should be considered during any decision concerning treatment. Our results show that the newly developed ALBI score can help differentiate a distinct subgroup of patients (ALBI2) within Child’s A patients who do not gain survival benefit from liver resection. MWA provided a significantly better short term peri-operative outcome and long term overall survival than liver resection. For patients with good liver function, Child’s A and ALBI 1, liver resection provided better overall survival than MWA.

Whether local ablation or liver resection should be the treatment for early HCC remains controversial. The controversy surrounds (1) what is the best ablative modality and (2) which patients will gain benefit from local ablation. Radiofrequency ablation is currently the most commonly used ablative method. MWA has received increased attention in recent years because of advances in technology leading to several potential advantage over RFA. The heating by microwave is primarily active and the transmission of microwaves in the living tissue is not limited by tissue desiccation and charring. When compared with RFA, it can create a larger ablation volume in a shorter ablation time.10, 13, 18-21 There is no heat sink effect and no earth plate injury. Other advantages include consistently higher intra-tumoral temperatures, deeper penetration of microwave energy and propagation across poorly conductive tissue.

Retrospective studies and meta-analyses have shown that microwave ablation (MWA) is at least as effective as, if not superior to, radiofrequency ablation in treating HCC. 14, 15 Nevertheless, whether the performance of MWA is comparable to that of the gold standard treatment, i.e. liver resection, remains unknown. Reports comparing these two treatments are scarce in the current literature. Our study tried to answer two major questions in the management of HCC: 1) what is the performance of MWA when compared with liver resection as a treatment for early HCC; and 2) how to define a degree of liver function that impacts adversely on liver resection. Our results suggest that liver resection provides a lower local recurrence rate, better overall survival and disease-free survivals in patients with good liver function, i.e. Child’s A, ALBI1, and should be the treatment of choice in this group of patients. For patients outside this category, even though they were Child’s A, MWA provided better overall survival without an increase in the local recurrence rate. MWA was also associated with less intra-operative blood loss and lower complication rates, which are known risk factors for poor prognosis after hepatectomy. 22-24

It is well-accepted that liver resection should be the treatment of choice in patients with good liver function while local ablation should be considered in patients with poor background liver function. Various scoring systems are currently used to define the extent of liver dysfunction. The Child-Pugh score is the most commonly used scoring system for gauging the severity of hepatic dysfunction in patients with HCC and has been incorporated into most HCC staging systems including the Barcelona Clinic Liver Cancer (BCLC) system, which also recommends treatment. However, two out of the five parameters are clinical parameters (ascites and encephalopathy) which are highly subjective. The model for end-stage liver disease (MELD) score is specifically designed for patients with end-stage liver disease. Patients with HCC scheduled for liver resection are usually with apparently good liver function, and seldom have ‘end stage liver disease’. ICG clearance test and volumetric studies by sectional imaging are technically troublesome. Most of the patients subjected to liver resection will have good ICG results. Volumetric studies only provide information on volume, but not the functional status. Indeed, none of the currently available methods of liver function assessment can accurately definite the degree of liver (dys)function that significantly impacts on the outcome of resection.

The albumin-bilirubin (ALBI) score is simpler and a more objective alternative to the Child-Pugh score.1 The score is calculated from the serum albumin and bilirubin concentrations and is thus, entirely objective. The score is a continuous variable that can then be categorized into three distinct grades, ALBI 1, 2 and 3. The ALBI grade can be easily estimated using a heat map or a nomogram provided in the original publication. 1 Although it was developed based on variables representing liver functions only, it was independently associated with survivals and was validated in large databases of patients from different countries. When incorporated into various staging systems it has superior or similar overall prognostic discrimination compared to when liver dysfunction is assessed by the Child-Pugh score. 3-5

Liver function impacts on long-term survival for patients HCC undergoing curative therapy. According to international guidelines, liver resection should be confined to those with Child-Pugh grade A in order to avoid the life-threatening complications associated with poor liver function. 8, 25, 26 We have previously shown that there are two distinct subgroups as classified by the ALBI score within Child-Pugh grade A. 2 Among patients undergoing liver resection, the survival of patients with ALBI grade 1 was about twice as long as those with ALBI grade 2 and such differences were consistent across different countries. Results in patients undergoing ablative therapies were similar. Such information may influence the decision to resect or ablate. The present study suggests that the ALBI grade has a potential role in patient selection for treatment. Among patients with Child-Pugh grade A, liver resection appears to provide survival benefit only in patients with good liver function as classified by ALBI grade 1. Liver resection should still be the treatment of choice in this group of patients. For patients with ALBI grade 2 within the Child-Pugh grade A, MWA provides a significantly better overall survival. Furthermore, a significant higher proportional of patients could receive treatment for local recurrence after MWA. It could be a result of better reservation of liver function after MWA. On the other hand, liver resection is associated with a significantly higher complication rate and operative blood loss. Both are known risk factors for poor prognosis. MWA could be considered as treatment of choice in this group of patients if liver transplant is not an option.

The strengths of our study include provision of direct comparison of MWA and liver resection in a relatively well-matched sample and demonstration of the clinical application of the newly developed ALBI score in patient selection of treatment. In order to study the true merit of MWA, a comparison with gold standard (liver resection) is necessary. Ideally, this question should be answered by a prospective randomized controlled study. However, according to our knowledge, there are no such studies reported in the current literature.

Limitations of our study include its retrospective nature and the small number of patients in the subgroup analysis. Moreover, this study is limited to Chinese patients. Results should be confirmed by a prospective randomized controlled trial with a larger sample size and involving other populations.

In conclusion, the ALBI grade can be used in patient selection and stratification when considering MWA or liver resection as a treatment for HCC. In patients with Child’s A cirrhosis, there exists a distinct subgroup of patients with liver dysfunction (ALBI 2) in whom MWA provides better overall survival than liver resection. Results from this study forms a sound basis for a prospective randomised trial.

**References:**

1. Johnson PJ, Berhane S, Kagebayashi C, Satoura S, Teng M, Reeves HL, et al. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. J Clin Oncol 2015;**33**:550-8.
2. Toyoda H, Lai PB, O'Beirne J, Chong CC, Berhane S, Reeves H, et al. Long-term impact of liver function on curative therapy for hepatocellular carcinoma: application of the ALBI grade. Br J Cancer 2016;**114**:744-50.
3. Chan AW, Chong CC, Mo FK, Wong J, Yeo W, Johnson PJ, et al. Applicability of Albumin-Bilirubin-based Japan Integrated Staging (ALBI-T) score in hepatitis B-associated hepatocellular carcinoma. J Gastroenterol Hepatol 2016;**31**:1766-72.
4. Chan AW, Kumada T, Toyoda H, Tada T, Chong CC, Mo FK, et al. Integration of albumin-bilirubin (ALBI) score into Barcelona Clinic Liver Cancer (BCLC) system for hepatocellular carcinoma. J Gastroenterol Hepatol 2016;**31**:1300-6.
5. Chan AW, Chong CC, Mo FK, Wong J, Yeo W, Johnson PJ, et al. Incorporating albumin-bilirubin grade into the cancer of the liver Italian program system for hepatocellular carcinoma. J Gastroenterol Hepatol 2017;**32**:221-8.
6. Yau T, Tang VY, Yao TJ, Fan ST, Lo CM, Poon RT. Development of Hong Kong Liver Cancer staging system with treatment stratification for patients with hepatocellular carcinoma. Gastroenterology 2014;**146**:1691-700.
7. Han KH, Kudo M, Ye SL, Choi JY, Poon RT, Seong J, et al. Asian consensus workshop report: expert consensus guideline for the management of intermediate and advanced hepatocellular carcinoma in Asia. Oncology 2011;**81 Suppl 1**:158-64.
8. Bruix J, Reig M, Sherman M. Evidence-Based Diagnosis, Staging, and Treatment of Patients With Hepatocellular Carcinoma. Gastroenterology 2016;**150**:835-53.
9. Lee KF, Hui JW, Cheung YS, Wong JS, Chong CN, Wong J, et al. Surgical ablation of hepatocellular carcinoma with 2.45-GHz microwave: a critical appraisal of treatment outcomes. Hong Kong Med J 2012;**18**:85-91.
10. Liang P, Wang Y. Microwave ablation of hepatocellular carcinoma. Oncology 2007;**72 Suppl 1**:124-31.
11. Lloyd DM, Lau KN, Welsh F, Lee KF, Sherlock DJ, Choti MA, et al. International multicentre prospective study on microwave ablation of liver tumours: preliminary results. HPB (Oxford) 2011;**13**:579-85.
12. Lee KF, Wong J, Hui JW, Cheung YS, Chong CC, Fong AK, et al. Long-term outcomes of microwave versus radiofrequency ablation for hepatocellular carcinoma by surgical approach: A retrospective comparative study. Asian J Surg 2017;**40**:301-8.
13. Martin RC, Scoggins CR, McMasters KM. Safety and efficacy of microwave ablation of hepatic tumors: a prospective review of a 5-year experience. Ann Surg Oncol 2010;**17**:171-8.
14. Abdelaziz A, Elbaz T, Shousha HI, Mahmoud S, Ibrahim M, Abdelmaksoud A, et al. Efficacy and survival analysis of percutaneous radiofrequency versus microwave ablation for hepatocellular carcinoma: an Egyptian multidisciplinary clinic experience. Surg Endosc 2014;**28**:3429-34.
15. Facciorusso A, Di Maso M, Muscatiello N. Microwave ablation versus radiofrequency ablation for the treatment of hepatocellular carcinoma: A systematic review and meta-analysis. Int J Hyperthermia 2016;**32**:339-44.
16. Chong CC, Wong GL, Chan AW, Wong VW, Fong AK, Cheung YS, et al. Liver Stiffness Measurement Predicts High-grade Post-hepatectomy Liver Failure: A Prospective Cohort Study. J Gastroenterol Hepatol 2017;**32**:506-14.
17. Chong CC, Lee KF, Ip PC, Wong JS, Cheung SY, Wong J, et al. Pre-operative predictors of post-hepatectomy recurrence of hepatocellular carcinoma: can we predict earlier? Surgeon 2012;**10**:260-6.
18. Ong SL, Gravante G, Metcalfe MS, Strickland AD, Dennison AR, Lloyd DM. Efficacy and safety of microwave ablation for primary and secondary liver malignancies: a systematic review. Eur J Gastroenterol Hepatol 2009;**21**:599-605.
19. Iannitti DA, Martin RC, Simon CJ, Hope WW, Newcomb WL, McMasters KM, et al. Hepatic tumor ablation with clustered microwave antennae: the US Phase II trial. HPB (Oxford) 2007;**9**:120-4.
20. Jagad RB, Koshariya M, Kawamoto J, Papastratis P, Kefalourous H, Patris V, et al. Laparoscopic microwave ablation of liver tumors: our experience. Hepatogastroenterology 2008;**55**:27-32.
21. Bhardwaj N, Strickland AD, Ahmad F, El-Abassy M, Morgan B, Robertson GS, et al. Microwave ablation for unresectable hepatic tumours: clinical results using a novel microwave probe and generator. Eur J Surg Oncol 2010;**36**:264-8.
22. Chok KS, Ng KK, Poon RT, Lo CM, Fan ST. Impact of postoperative complications on long-term outcome of curative resection for hepatocellular carcinoma. Br J Surg 2009;**96**:81-7.
23. Katz SC, Shia J, Liau KH, Gonen M, Ruo L, Jarnagin WR, et al. Operative blood loss independently predicts recurrence and survival after resection of hepatocellular carcinoma. Ann Surg 2009;**249**:617-23.
24. Chikamoto A, Beppu T, Masuda T, Otao R, Okabe H, Hayashi H, et al. Amount of operative blood loss affects the long-term outcome after liver resection for hepatocellular carcinoma. Hepatogastroenterology 2012;**59**:1213-6.
25. Tsochatzis E, Meyer T, O'Beirne J, Burroughs AK. Transarterial chemoembolisation is not superior to embolisation alone: the recent European Association for the Study of the Liver (EASL) - European Organisation for Research and Treatment of Cancer (EORTC) guidelines. Eur J Cancer 2013;**49**:1509-10.
26. Omata M, Lesmana LA, Tateishi R, Chen PJ, Lin SM, Yoshida H, et al. Asian Pacific Association for the Study of the Liver consensus recommendations on hepatocellular carcinoma. Hepatol Int 2010;**4**:439-74.

**Table 1 Baseline characteristics before and after propensity score matching of patients underwent microwave ablation or liver resection**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Before Matching** | | **P-value** | **After Matching** | | **P-value** |
| **Microwave Ablation** **(n=63 )** | **Liver Resection** **(n=379 )** | **Microwave Ablation** **(n=63)** | **Liver Resection** **(n=63)** |
| Age (years)# | 63.9 (9.0) | 58.5 (9.9) | ***<0.001*** | 63.9 (9.0) | 63.8 (8.6) | 0.903 |
| Male Sex\* | 44 (69.8) | 325 (85.8) | ***0.002*** | 44 (69.8) | 46 (73.0) | 0.693 |
| Hepatitis B carrier\* | 50 (79.4) | 309 (81.5) | 0.684 | 50 (79.4) | 54 (85.7) | 0.348 |
| Hepatitis C carrier\* | 6 (9.5) | 24 (6.3) | 0.413 | 6 (9.5) | 4 (6.3) | 0.510 |
| Number of Comorbidity# | 1.3 (1.2) | 1.3 (1.4) | 0.832 | 1.3 (1.2) | 1.4 (1.3) | 0.675 |
| Child’s grading A\* | 57 (90.5) | 366 (96.6) | ***0.040*** | 57 (90.5) | 59 (93.7) | 0.510 |
| Cirrhosis\* | 57 (90.5) | 216 (57.0) | ***<0.001*** | 57 (90.5) | 58 (92.1) | 0.752 |
| Platelet counts (109/l) # | 105.2 (50.6) | 172.1 (79.0) | ***<0.001*** | 105.2 (50.6) | 115.2 (41.6) | 0.227 |
| Bilirubin (umol/l)# | 16.5 (8.1) | 11.4 (6.9) | ***<0.001*** | 16.5 (8.1) | 14.4 (10.9) | 0.215 |
| Albumin (g/l)# | 39.0 (4.6) | 41.0 (4.7) | ***0.002*** | 39.0 (4.6) | 40.1 (4.9) | 0.175 |
| INR# | 1.1 (0.1) | 1.0 (0.1) | ***<0.001*** | 1.1 (0.1) | 1.1 (0.1) | 0.329 |
| ALP (IU/l)# | 93.4 (39.1) | 91.7 (47.4) | 0.792 | 93.4 (39.1) | 94.1 (60.8) | 0.943 |
| Creatinine ªumol/l)# | 85.1 (22.8) | 84.1 (38.3) | 0.854 | 85.1 (22.8) | 82.4 (20.3) | 0.500 |
| AFP (ng/ml)# | 224.5 (609.9) | 5133.3 (38490.3) | 0.314 | 224.5 (609.9) | 291.7 ( 830.0) | 0.717 |
| MELD <=10\* | 49 (77.8) | 354 (93.4) | ***<0.001*** | 49 (77.8) | 53 (84.1) | 0.364 |
| ALBI ( 1 vs 2/3)\* | 33 (52.4) vs 30 (47.6) | 288 (76.0) vs (25 (6.6) | ***<0.001*** | 33 (52.4) vs 30 (47.6) | 41 (65.1) vs 22 (34.9) | 0.148 |

\*Categorical Data presented in n (%)

#Continuous data presented in mean (standard deviation)

INR: International Ratio; ALP: Alkaline Phosphatase; AFP: Alpha-Fetoprotein; MELD: Model for End-stage Liver Disease

**Table 2 Clinicopathological parameters for patients with ALBI grade 1 underwent microwave ablation and liver resection**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Microwave Ablation**  **(n = 33)** | **Liver Resection**  **(n = 41)** | **P-value** |
| Age (years)# | 65.9 (9.9) | 63.5 (8.4) | 0.252 |
| Male Sex\* | 25 (75.8) | 27 (65.9) | 0.354 |
| Hepatitis B carrier\* | 26 (78.8) | 38 (92.7) | 0.099 |
| Hepatitis C carrier\* | 1 (3.0) | 1 (2.4) | >0.999 |
| Number of Comorbidity# | 1.3 (1.2) | 1.1 (1.3) | 0.597 |
| Child’s grading A\* | 30 (90.9) | 41 (100.0) | 0.084 |
| Cirrhosis\* | 28 (84.8) | 37 (90.2) | 0.501 |
| Platelet counts (109/l) # | 128.6 (54.5) | 124.6 (44.2) | 0.723 |
| Bilirubin (umol/l)# | 12.4 (5.1) | 11.1 (4.3) | 0.246 |
| Albumin (g/l)# | 42.1 (2.9) | 42.8 (2.9) | 0.319 |
| INR# | 1.1 (0.1) | 1.1 (0.1) | 0.537 |
| ALP (IU/l)# | 85.6 (33.1) | 80.4 (24.1) | 0.456 |
| Creatinine (umol/l)# | 88.4 (17.4) | 85.7 (22.1) | 0.558 |
| AFP (ng/ml)# | 411.9 (799.0) | 267.5 (578.5) | 0.371 |
| MELD <=10\* | 29 (87.9) | 38 (92.7) | 0.693 |
| Solitary Tumour\* | 32 (97.0) | 41 (100.0) | 0.446 |
| Tumour Size (cm)# | 3.2 (0.8) | 3.2 (1.5) | 0.904 |

\*Categorical Data presented in n (%)

#Continuous data presented in mean (standard deviation)

ALBI: Albumin-bilirubin; INR: International Ratio; ALP: Alkaline Phosphatase; AFP: Alpha-Fetoprotein; MELD: Model for End-stage Liver Disease

**Table 3 Clinicopathological parameters for patients with ALBI grade 2/3 underwent microwave ablation and liver resection**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Microwave Ablation**  **(n = 30)** | **Liver Resection**  **(n = 22)** | **P-value** |
| Age (years)# | 61.7 (7.4) | 64.2 (9.1) | 0.281 |
| Male Sex\* | 19 (63.3) | 19 (86.4) | 0.064 |
| Hepatitis B carrier\* | 24 (80.0) | 68 (72.7) | 0.539 |
| Hepatitis C carrier\* | 5 (16.7) | 3 (13.6) | >0.999 |
| Number of Comorbidity# | 1.3 (1.3) | 1.8 (1.3) | 0.138 |
| Child’s grading A\* | 27 (90.0) | 18 (81.8) | 0.438 |
| Cirrhosis\* | 29 (96.7) | 21 (95.5) | >0.999 |
| Platelet counts (109/l)# | 79.4 (29.8) | 97.8 (30.2) | ***0.033*** |
| Bilirubin (umol/l)# | 21.0 (8.4) | 20.5 (16.0) | 0.878 |
| Albumin (g/l)# | 35.5 (3.6) | 35.2 (3.9) | 0.738 |
| INR# | 1.17 (0.14) | 1.17 (0.14) | 0.974 |
| ALP (IU/l)# | 102.0 (43.7) | 119.4 (93.7) | 0.374 |
| Creatinine ªumol/l)# | 81.4 (27.4) | 76.5 (15.1) | 0.447 |
| AFP (ng/ml)# | 60.5 (154.2) | 336.7 (1180.0) | 0.287 |
| MELD <=10\* | 20 (66.7) | 15 (68.2) | 0.908 |
| Solitary Tumour\* | 27 (90.0) | 18 (81.8) | 0.438 |
| Tumour Size (cm)# | 3.4 (0.9) | 4.2 (3.6) | 0.309 |

\*Categorical Data presented in n (%)

#Continuous data presented in mean (standard deviation)

ALBI: Albumin-bilirubin; INR: International Ratio; ALP: Alkaline Phosphatase; AFP: Alpha-Fetoprotein; MELD: Model for End-stage Liver Disease

**Table 4 Baseline characteristics before and after propensity score matching of patients with Child’s A and ALBI grade 2 underwent microwave ablation or liver resection**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Before Matching** | | **P-value** | **After Matching** | | **P-value** |
| **Microwave Ablation**  **(n = 27 )** | **Liver Resection**  **(n = 78 )** | **Microwave Ablation**  **(n = 27)** | **Liver Resection**  **(n = 27)** |
| Age (years)# | 62.0 (7.1) | 61.0 (10.6) | 0.625 | 62.0 (7.1) | 62.7 (10.3) | 0.795 |
| Male Sex\* | 17 (63.0) | 66 (84.6) | ***0.017*** | 17 (63.0) | 21 (77.8) | 0.233 |
| Hepatitis B carrier\* | 22 (81.5) | 57 (73.1) | 0.383 | 22 (81.5) | 21 (77.8) | 0.735 |
| Hepatitis C carrier\* | 4 (14.8) | 8 (10.3) | 0.500 | 4 (14.8) | 3 (11.1) | >0.999 |
| Number of Comorbidity# | 1.3 (1.3) | 1.6 (14.5) | 0.416 | 1.3 (1.3) | 1.7 (1.4) | 0.279 |
| Cirrhosis\* | 26 (96.3) | 42 (53.8) | ***<0.001*** | 26 (96.3) | 25 (92.6) | >0.999 |
| Platelet counts (109/l)# | 80.2 (30.9) | 186.8 (126.1) | ***<0.001*** | 80.2 (30.9) | 139.3 (112.7) | ***0.011*** |
| Bilirubin (umol/l)# | 21.3 (8.6) | 13.5 (8.1) | ***<0.001*** | 21.3 (8.6) | 14.7 (8.5) | ***0.006*** |
| Albumin (g/l)# | 35.9 (3.6) | 35.7 (2.9) | 0.786 | 35.9 (3.6) | 36.8 (2.1) | 0.256 |
| INR# | 1.2 (0.1) | 1.1 (0.1) | ***0.019*** | 1.2 (0.1) | 1.1 (0.1) | 0.757 |
| ALP (IU/l)# | 99.6 (44.0) | 103.7 (53.2) | 0.717 | 99.6 (44.0) | 100.9 (50.2) | 0.922 |
| Creatinine ªumol/l)# | 82.4 (28.0) | 81.0 (27.2) | 0.810 | 82.4 (28.0) | 76.3 (17.5) | 0.335 |
| AFP (ng/ml)# | 63.4 (162.1) | 6786.4 (32238.0) | 0.073 | 63.4 (162.1) | 83.7 (174.6) | 0.659 |
| MELD <=10\* | 19 (70.4) | 66 (84.6) | 0.140 | 19 (70.4) | 22 (81.5) | 0.340 |
| Solitary Tumour\* | 25 (92.6) | 49 (62.8) | ***0.003*** | 25 (92.6) | 25 (92.6) | >0.999 |
| Tumour Size (cm)# | 3.4 (1.0) | 6.5 (4.8) | ***<0.001*** | 3.4 (1.0) | 3.8 (2.6) | 0.476 |

\*Categorical Data presented in n (%)

#Continuous data presented in mean (standard deviation)

ALBI: Albumin-bilirubin; INR: International Ratio; ALP: Alkaline Phosphatase; AFP: Alpha-Fetoprotein; MELD: Model for End-stage Liver Disease

**Table 5 Outcomes of patients underwent microwave ablation or liver resection**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Microwave Ablation** | **Liver Resection** | **P-value** |
| **63 matched-pairs of patients** | **N = 63** | **N = 63** |  |
| Postoperative length of stay (day)# | 5.0 (2.2) | 8.6 (6.9) | ***0.002*** |
| Blood loss (ml)# | 29.4 (34.7) | 407.3 (402.8) | ***<0.001*** |
| Blood transfusion\* | 2 (6.1) | 1 (2.4) | 0.583 |
| Complications\* | 4 (12.1) | 9 (22.0) | 0.362 |
| 30 Days mortality\* | 0 (0.0) | 0 (0.0) | NA |
| 90 Days mortality\* | 0 (0.0) | 0 (0.0) | NA |
| **Local Intrahepatic recurrence** | **2 (7.4%)** | **0 (0%)** | **0.491** |
|  |  |  |  |
| **Patients with ALBI grade 1** | **N = 33** | **N =41** |  |
| Postoperative length of stay (day)# | 5.0 (2.2) | 8.6 (6.9) | ***0.002*** |
| Blood loss (ml)# | 29.4 (34.7) | 407.3 (402.8) | ***<0.001*** |
| Blood transfusion\* | 2 (6.1) | 1 (2.4) | 0.583 |
| Complications\* | 4 (12.1) | 9 (22.0) | 0.362 |
| 30 Days mortality\* | 0 (0.0) | 0 (0.0) | NA |
| 90 Days mortality\* | 0 (0.0) | 0 (0.0) | NA |
|  |  |  |  |
| **Patients with ALBI grade 2 or 3** | **N = 30** | **N = 22** |  |
| Postoperative length of stay (day)# | 5.1 (2.6) | 9.8 (5.6) | ***0.001*** |
| Blood loss (ml)# | 30.8 (61.7) | 836.1 (1042.2) | ***0.002*** |
| Blood transfusion\* | 0 (0.0) | 2 (9.1) | 0.174 |
| Complications\* | 2 (6.7) | 11 (50.0) | ***<0.001*** |
| 30 Days mortality\* | 0 (0.0) | 1 (4.5) | 0.423 |
| 90 Days mortality\* | 1 (3.3) | 3 (13.6) | 0.299 |
|  |  |  |  |
| **27 matched-pairs of patients with Child’s A and ALBI grade 2** | **N =27** | **N = 27** |  |
| Postoperative length of stay (day)# | 5.1 (2.6) | 8.8 (4.6) | 0***.001*** |
| Blood loss (ml)# | 31.3 (64.1) | 530.5 (544.8) | ***<0.001*** |
| Blood transfusion\* | 0 (0.0) | 2 (7.4) | 0.491 |
| Complications\* | 2 (7.4) | 11 (40.7) | ***0.004*** |
| 30 Days mortality\* | 0 (0.0) | 1 (3.7) | >0.999 |
| 90 Days mortality\* | 1 (3.7) | 2 (7.4) | >0.999 |

\*Categorical Data presented in n(%)

#Continuous data presented in mean (standard deviation)

NA: Not applicable; ALBI: Albumin-bilirubin;

**Figures Legends**

**Figure 1** Kaplan-Meier survival plots comparing (A) overall survival (p=0.186) and (B) disease-free survival (p<0.001) among the 63 matched-pairs of patients undergoing microwave ablation or liver resection.

**Figure 2** Kaplan-Meier survival plots comparing (A) overall survival (p = 0.043) and (B) disease-free survival (p = 0.457) among patients with Child’s A and Albumin-bilirubin Grade 2 undergoing microwave ablation or liver resection.