CLINICAL STUDY

Microwave Ablation as Bridging to Liver Transplant for Patients with Hepatocellular Carcinoma: A Single-Center Retrospective Analysis

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ABSTRACT

Purpose: To evaluate the efficacy and safety of microwave (MW) ablation as first-line locoregional therapy (LRT) for bridging patients with hepatocellular carcinoma (HCC) to liver transplant.

Materials and Methods: This retrospective study evaluated 88 patients who received percutaneous MW ablation for 141 tumors as first-line LRT for HCC and who were listed for liver transplantation at a single medical center between 2011 and 2019. The overall survival (OS) rate statuses after liver transplant, waitlist retention, and disease progression were evaluated using the Kaplan-Meier techniques.

Results: Among the 88 patients (72 men and 16 women; mean age, 60 years; Model for End-Stage Liver Disease score, 11.2) who were listed for transplant, the median waitlist time was 9.4 months (interquartile range, 5.5–18.9). Seventy-one (80.7%) patients received transplant after a median waitlist time of 8.5 months. Seventeen (19.3%) patients were removed from the waitlist; of these, 4 (4.5%) were removed because of tumors outside of the Milan criteria (HCC-specific dropout). No difference in tumor size or alpha-fetoprotein was observed in the transplanted versus nontransplanted patients at the time of ablation (2.1 vs 2.1 cm and 34.4 vs 34.7 ng/mL for transplanted vs nontransplanted, respectively; $P > .05$). Five (5.1%) of the 88 patients experienced adverse events after ablation; however, they all recovered. There were no cases of tract seeding. The local tumor progression (LTP) rate was 7.2%. The OS status after liver transplant at 5 years was 76.7%, and the disease-specific survival after LTP was 89.6%, with a median follow-up of 61 months for all patients.

Conclusions: MW ablation appears to be safe and effective for bridging patients with HCC to liver transplant without waitlist removal from seeding, adverse events, or LTP.

ABBREVIATIONS

AFP = alpha-fetoprotein, CT = computed tomography, DSS = disease-specific survival, HCC = hepatocellular carcinoma, IQR = interquartile range, LRT = locoregional therapy, LTP = local tumor progression, MW = microwave, OS = overall survival, RF = radiofrequency, RFS = recurrence-free survival, TACE = transarterial chemoembolization, Y-90 = yttrium-90

Hepatocellular carcinoma (HCC) is the fastest-growing cause of cancer-related death in the United States (1). Liver transplantation is the only treatment option that potentially cures HCC and the underlying cirrhosis; however, the limited availability of donors results in prolonged waitlist times, increasing the risk of cancer progression beyond transplant eligibility (2–6). The incidence of HCC progression for patients who do not receive locoregional therapy (LRT) while listed for transplantation is reported to be 10%–23% but can be as high as 88%, with waitlist dropout rates at 6 and 12 months of approximately 12% and 30%, respectively (1,2,6).

There is growing evidence that bridging with LRT increases waitlist retention, posttransplant disease-specific survival (DSS), and overall survival (OS) (4–9). Both ablative and transarterial therapies have been successfully used for bridging; however, there is no consensus on the first-line modality in cases that are amenable to both (7,10,11). For ablation candidates, there is an increased

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RESEARCH HIGHLIGHTS

- Patients with hepatocelllular carcinoma who were treated with microwave ablation and listed for transplantation were reviewed. Of the 88 patients, 80.7% (71) eventually went on to receive a liver transplant during the study period, with no deaths while awaiting transplantation.
- Tumor growth outside of the Milan criteria resulting in dropout (hepatocellular carcinoma [HCC]-specific dropout) was 4.5% (4/88), and all 4 patients with HCC-specific dropout were removed because of the development of new multifocal HCC separate from the site of ablation.
- Five (7.0%) of 71 patients had posttransplant recurrence of HCC, and all died during the study period.
- The overall adverse event rate was 5.1% (5/99), with a major adverse event rate of 3.0% (3/99).

STUDY DETAILS

Study type: Retrospective, observational, descriptive study

Level of evidence: 4 (SIR-D)

interest in microwave (MW) over radiofrequency (RF) because of higher applied temperatures, faster heating, larger ablation zones, and high local control rates (8,12,13).

The ideal bridging strategy decreases waitlist dropout from tumor progression and has few adverse events and a high OS after transplant. To date, most LRT bridging studies (2,14) have demonstrated some of these characteristics; however, comparisons are limited, and there is a paucity of data on MW ablation for this objective. This single-center, retrospective study aimed to evaluate the efficacy and safety of MW ablation as first-line LRT for bridging patients with HCC to transplant.

MATERIALS AND METHODS

Data Collection and Patients

Institutional review board at the University of Wisconsin approval was obtained to deidentify a database for research purposes, and a waiver of informed consent was granted for this retrospective study. Patients who were bridged to transplant with MW between 2011 and 2019 were identified, defined as patients with an HCC diagnosis who were listed for liver transplantation and who received MW ablation for the purpose of waitlist retention. A minority (n = 37) was included in a previous publication (15) comparing RF and MW. Imaging and clinical data were collected from an institutional database and electronic medical records. The terminology and reporting criteria followed previously established standards (16). No patients were excluded. Patients were selected for bridging during multidisciplinary liver tumor conference, which generally followed the Barcelona Clinic Liver Cancer guidelines for patients staged 0 or A (17). All patients were within the Milan criteria at the time of ablation with one exception (5.3-cm HCC); therefore, the analysis of downstaging is beyond the scope of this study. The study site is in the United Network for Organ Sharing region 7, where the current median waitlist time for deceased donor liver transplant is 13.5 months (18).

A total of 88 patients (72 men and 16 women) with HCC underwent 99 MW sessions to treat 141 tumors for bridging to transplant. Patient demographics, cause of liver disease, alpha-fetoprotein (AFP), and Model for End-Stage Liver Disease scores are summarized in Table 1. The mean age was 60 years ± 6, with a mean native Model for End-Stage Liver Disease score of 11.2 ± 3.7. One patient with bilobar disease had incomplete treatment because of poor liver function and a risk of decompensation. Another patient with 2 tumors had MW and ethanol ablation to one because of the proximity to the common bile duct. Only the MW lesion was used to calculate local tumor progression (LTP). Combination therapy with transarterial chemoembolization and MW ablation (TACE + MW) was used for 3 patients. Additional non-MW LRT was used in 13 patients after the initial MW treatment and included TACE (n = 3), yttrium-90 (Y-90) (n = 8), stereotactic body radiation therapy (n = 1), and TACE + stereotactic body radiation therapy (n = 1).

The mean tumor size was 2.1 cm ± 0.8 (range, 0.5–5.3 cm), with 91% (129) of 141 tumors having a size of <3 cm and a median of 1 tumor treated per session (range, 1–3). The median AFP level before transplant was 5.6 ng/mL; 1 patient had an AFP level of >100 ng/mL.

Ablation Procedure

All MW treatments were performed at a single center by radiologists with 1–25 years of ablation experience (8,12). Patients were placed on a computed tomography (CT) table (Optima 560 Wide Bore; GE Medical, Waukesha, Wisconsin) and underwent general anesthesia. Ultrasound was the primary imaging modality for probe placement (E9/E10; GE Medical) with CT confirmation. MW ablation was performed using a 140-W gas-cooled system with in-phase power delivery to 1–3 antennas (NeuWave Microwave Ablation Systems; Ethicon, Madison, Wisconsin). The number and placement of antennas, time, and power were decided by the operating physician at the time of procedure. Ablations were monitored in real time using ultrasound with the intent of producing a concentric ablation margin of 5–10 mm beyond the visible tumor. After completion of the ablation and probe withdrawal, contrast-enhanced CT was performed and the images were compared with preprocedural images. Cases in which incomplete treatment or inadequate margins were suspected on the basis of postprocedural contrast-enhanced CT were immediately retreated at the same session.

Table 1. Patient Demographics

Variables	All patients	Transplanted	Removed from waitlist
Number (% total)	88	71 (81)	17 (19)
Sex (M/F)	72/16	59/12	13/4
Age (mean y)	59	60	59
Cause of cirrhosis, n (%)			
Hepatitis C	35 (40)	32 (45)	3 (18)
ALD	23 (26)	18 (25)	5 (29)
Hepatitis C + ALD	14 (16)	7 (10)	7 (41)
NASH	10 (11)	10 (14)	0 (0)
Other	6 (7)	4 (6)	2 (12)
MELD at ablation,* n (%)			
<15	71 (84)	57 (81)	14 (82)
15–29	14 (16)	13 (19)	1 (6)
>30	0 (0)	0 (0)	0 (0)
Mean MELD score at ablation, mean ± SD	11.2 ± 3.7	11.4 ± 3.9	10.3 ± 2.6
Tumor size, mean (cm) ± SD	2.1 ± 0.8	2.1 ± 0.8	2.1 ± 0.8
≥3 cm	15 (11%)	12 (10%)	3 (12%)
AFP at ablation (mean ± SD, ng/mL)	34.4 ± 61.7	34.7 ± 55.4	32.6 ± 84.7
BCLC stage (0/A/B)	7/81/0	4/67/0	3/14/0

AFP = alpha-fetoprotein; ALD = alcohol-related liver disease; BCLC = Barcelona Clinic Liver Cancer; F = female; M = male; MELD = Model for End-Stage Liver Disease; NASH = nonalcoholic steatohepatitis.
*One transplanted patient and 2 patients removed from the waitlist did not have data available to calculate MELD scores.

Adverse Events and Patient Follow-Up

Adverse events were classified according to the Society of Interventional Radiology (SIR) guidelines (19). Patients were evaluated every 3 months for 1 year and then every 6 months with CT or magnetic resonance imaging to evaluate LTP and distant metastases. Patients who did not have subsequent imaging in the medical record were censored at the date of the last imaging follow-up.

Statistical Analysis

LTP was reported per tumor and per patient (16). Inferential statistical analysis was performed at the patient level, where each patient contributed one independent observation. The median follow-up was estimated using a reverse Kaplan-Meier technique. Waitlist retention, recurrence-free survival (RFS), OS, and DSS were estimated using the Kaplan-Meier method. For waitlist retention, the day the patient was listed for liver transplant was used as time 0. To analyze the waitlist retention data, a Fine-Gray competing risk model was estimated (20), where liver transplant was considered as a competing risk of waitlist dropout using the "cmprsk" package in R (V 2.2-10). No patients died on the waitlist; hence, death was not considered a competing event. In addition to LTP status, the largest tumor size, and AFP, this model also adjusted for patient age and sex. For RFS, OS, and DSS, the date of MW ablation was used as time 0, and events were defined as HCC recurrence after transplant or all-cause mortality, all-cause mortality, and HCC-specific mortality, respectively (16). A univariate logistic regression model tested the predictors of HCC-specific waitlist dropoff. Multivariate analysis was performed using the Cox proportional hazards model to test the predictors of shortened RFS, OS, and DSS, all 3 models were adjusted for both patient age and sex. The Cox model P values were derived using the 2-sided Wald tests, where the null hypothesis, H_0: $\beta = 0$, was tested against the alternative, H_1: $\beta = \emptyset$, for each coefficient. The proportional hazards assumption for each model was assessed using the score tests of the Schoenfeld residuals as implemented in the "survival" package. No model was found to have evidence of a significant departure from the proportional hazards assumption ($P > .05$ for all coefficients). Differences in AFP by recurrence status (among transplanted patients) were assessed using a nonparametric Wilcoxon rank-sum test. A P value of $<.05$ was considered significant for all results. Analyses were performed using R version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Adverse Events

There were no intraprocedural or postprocedural deaths within 30 days and no case of tumor seeding or bleeding needing intervention. The overall adverse event rate was 5.1% (5/99), with a major adverse event rate of 3.0% (3/99): (*a*) hypoxia following extubation requiring reintubation and intensive care unit admission (SIR category 4, n = 1), (*b*) peritonitis requiring paracenteses 20 days after ablation (SIR category 3, n = 1), and (*c*) acute kidney insufficiency and pneumonia with resolution (SIR category 3, n = 1). All 3 patients with major adverse events eventually underwent transplantation. There were 2 minor adverse events (bleeding contemporaneously cauterized with MW, SIR category 1, n = 2).

LTP and Additional LRT While Waitlisted

The primary rate of technical success was 100%. The overall LTP rates were 7.2% (10/138) per tumor and 11.6% (10/86) per patient (2 patients/3 tumors were excluded because of the lack of imaging before transplant). Of the 10 patients with LTP, 2 received repeat MW, 5 were treated with another LRT (TACE, Y-90, and radiation), 2 were transplanted without reintervention, and 1 dropped off the waitlist because of multifocal HCC. MW was successful in both retreated patients with LTP for a secondary LTP rate of 5.8% per tumor and 9.3% per patient. Of the 10 patients with LTP, 4 dropped off the transplant list, though none from failure to control the primary tumor. The small number of treatment failures limited statistical power to determine the risk factors for LTP.

Transplantation Waitlist Dynamics

The transplantation waitlist dynamics are provided in **Figure 1a**, **b**. The median waitlist time was 9.4 months

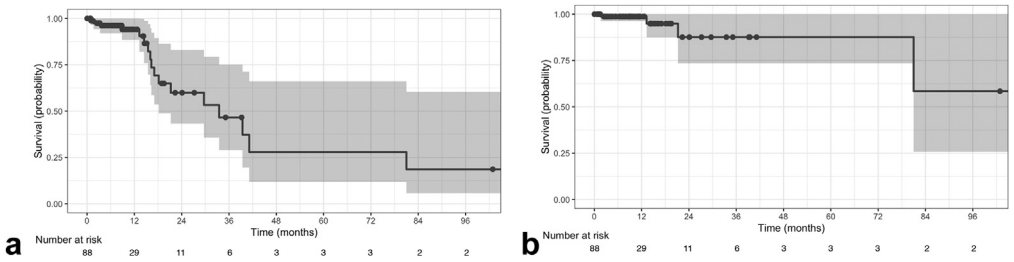

Figure 1. Kaplan-Meier survival analysis. **(a)** Eighty-eight patients who were listed for transplant were used to analyze removal from the waitlist. **(b)** Waitlist removal because of hepatocellular carcinoma progression was performed using all patients (n = 88) from the date of acceptance to waitlist to removal. Dots denoted the time of censoring. Time 0 was the date of waitlisting.

(interquartile range [IQR], 5.5–18.9 months). Transplanted patients had shorter waitlist times (median, 8.5 months; IQR, 4.5–11.6 months) than patients removed from the list (median, 16.1 months; IQR, 10.9–31.1 months). The median patient follow-up was 61 months (IQR, 39–86 months) for all patients.

Of the 88 patients listed for transplant, 80.7% (71) eventually received a deceased donor organ during the study period, resulting in an all-cause dropout of 19.3% (17/88). By 12 months and 3 and 5 years, 29 (33%), 6 (6.8%), and 3 (3.4%) of patients remained on the waitlist, respectively. There were no deaths while awaiting transplantation. Tumor growth outside of the Milan criteria causing HCC-specific dropout was 4.5% (4/88) (Table 2) at 2, 13, 21, and 80 months after the initial ablation (median, 17.0 months [IQR, 10.2–35.7 months] for HCC-specific dropout vs 15.9 months [IQR, 10.1–26.4 months] for non–HCC-specific dropout). All 4 patients with HCC-specific dropout were due to new multifocal HCC separate from the ablation site. AFP, tumor size, and LTP were not associated with an increased risk of dropout (univariate logistic regression, $P = .25$,.37, and.18, respectively). No patients were removed because of failure of local control of the index tumor.

Table 2. Indications for Removal from Waitlist

Indications for removal from waitlist	Number (% of all 88 patients)
Complete response to ablation	3 (3.4)
HCC progression outside of the Milan criteria	4 (4.5)
Continued substance use	3 (3.4)
Lack of social support	3 (3.4)
Worsening comorbidities	3 (3.4)
Self-withdrawal	1 (1.1)

HCC, hepatocellular carcinoma.

Table 3. Summary of Explanted Liver Pathology Reports

Explant	Percentage (n)
No residual HCC	49.3 (35/71)
Residual HCC	
Within Milan	35.2 (25/71)
Outside Milan	15.5 (11/71)
Moderately differentiated HCC	47.2 (19/36)
Well-differentiated HCC	52.8 (17/36)
Microvascular invasion	8.5 (6/71)

HCC = hepatocellular carcinoma.

Explant Liver Characteristics

Expant liver characteristics are summarized in Table 3. A total of 181 tumors were detected in the explant specimens (123 ablated and 58 not ablated). Of the 123 ablated tumors, 99 (80.5%) demonstrated complete pathologic necrosis with no viable tumor, and 24 (19.5%) had evidence of residual viable tumor. The remaining 58 tumors not targeted for ablation and discovered only at explant had a mean size of 0.99 cm (range, 0.2–3.3 cm). Per patient, 49.3% (35/71) had no residual tumors, 35.2% (25/71) had viable tumors but were within the Milan criteria, and 15.5% (11/71) had residual tumors that exceeded the Milan criteria. Of the explants with viable tumors, 47.2% (17/36) were moderately differentiated HCCs and 52.8% (19/36) were well-differentiated HCCs. Microvascular invasion was present in 8.5% (6/71) of explants. There was not enough detail in one pathology report to perform radiologic-pathologic correlation.

RFS, OS, and DSS

The OS rates of the population at 1, 3, and 5 years were 96.5%, 79.1%, and 70.4%, respectively (Fig 2). The DSS rates at 1, 3, and 5 years were 100%, 95.5%, and 89.1%, respectively (Fig 3).

For transplanted patients, at 1, 3, and 5 years, the RFS rates were 86.8%, 80.0%, and 75.4%; the OS rates were 97.2%, 85.1%, and 76.7%; and the DSS rates were 100%, 96.7%, and 89.6%, respectively (Figs 4, 5). Of the 71 transplanted patients, 15 died during the study period—5 from metastatic HCC, 3 from graft failure, 1 from adverse events of posttransplant transjugular intrahepatic portosystemic shunt creation, 2 from myocardial infarction, 3 from sepsis, and 1 from cryptococcal infection.

At 1, 3, and 5 years, the OS rates of the 17 patients who were removed from the waitlist were 93.8%, 50.2%, and 40.2%, and the DSS rates were 100%, 85.7%, and 85.7%,

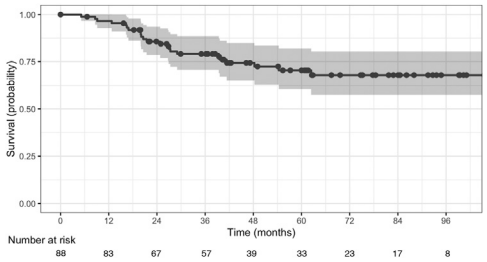

Figure 2. Kaplan-Meier survival analysis. All 88 patients who were waitlisted were used for overall survival analysis performed from the date of acceptance to the waiting list to the date of death from all causes. Dots denoted the time of censoring. Time 0 was the date of ablation.

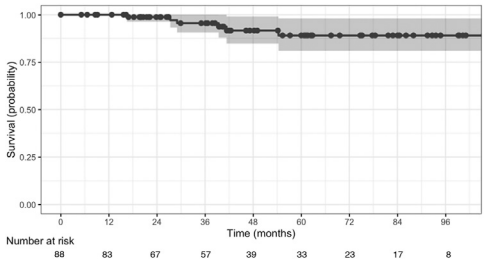

Figure 3. Kaplan-Meier survival analysis. Eighty-eight patients who were waitlisted for transplant were analyzed for disease-specific survival. Dots denoted the time of censoring. Time 0 was the date of ablation.

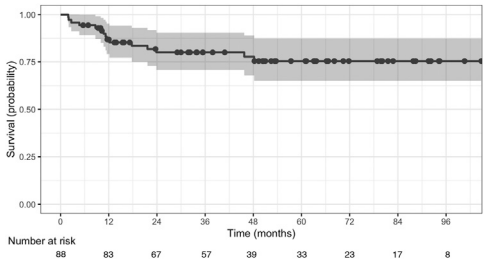

Figure 4. Kaplan-Meier survival analysis. Seventy-one patients who received transplantation were used to analyze postoperative recurrence-free survival, defined as the day of image-detected hepatocellular carcinoma recurrence. Dots denoted the time of censoring. Time 0 was the date of ablation.

respectively (Fig 5). The patients who exceeded the Milan criteria as the reason for waitlist removal had a 5-year OS of 0% compared with 56.6% for patients removed for other reasons.

The OS rates of the 11 patients who were found to be outside the Milan criteria on explantation were 100%, 77.1%, and 57.9%, and the DSS rates were 100%, 95.5%, and 89.1%, respectively (Figs 6, 7). Residual tumor on explant (either residual viable tumor at ablation site, new tumor detected at explant, or both) was not associated

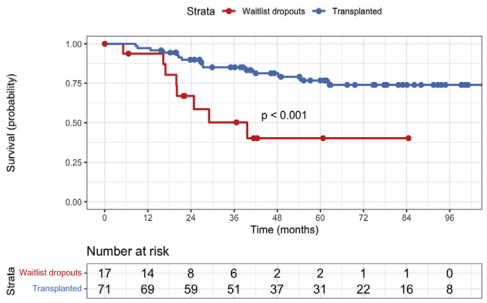

Figure 5. Kaplan-Meier survival analysis. Eighty-eight patients who were listed for transplant were used to analyze overall survival stratified by those who received transplant versus those who were removed from the waitlist. Dots denoted the time of censoring. Time 0 was the date of ablation.

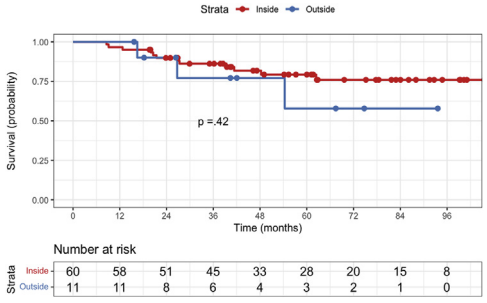

Figure 6. Kaplan-Meier survival analysis. Eleven patients who received transplantation and were determined to be outside the Milan criteria on explantation and 60 patients who were within the Milan criteria on explantation were used to analyze postoperative survival. Dots denoted the time of censoring. Time 0 was the date of ablation.

with decreased survival versus patients with no viable tumor ($P = .47$) (Fig 8). Larger tumor sizes were found to decrease DSS ($P = .01$) (Table 4).

HCC Recurrence after Transplantation

Five transplanted patients (5/71, 7.0%) died because of metastatic HCC. The mean size of ablated tumors (3.6 cm ± 1.3) in this subgroup was higher than the study mean (2.1 cm ± 0.8, $P = .0002$), and the mean waitlist time was 12 months (range, 3–24 months). The mean AFP in the 5 patients with metastatic disease was 55.2 ng/mL ± 43.2 versus 33.1 ng/mL ± 56.2 for patients without metastases ($P = .13$). Only one patient with HCC recurrence had microvascular invasion on explant. Two of the 5 patients with posttransplant recurrence had borderline enlarged lymph nodes at the time of ablation, which later proved to be metastatic nodes.

DISCUSSION

The primary goals of bridging are waitlist retention by preventing growth beyond the Milan criteria and improved HCC-specific survival after transplant (6,9,21). The results

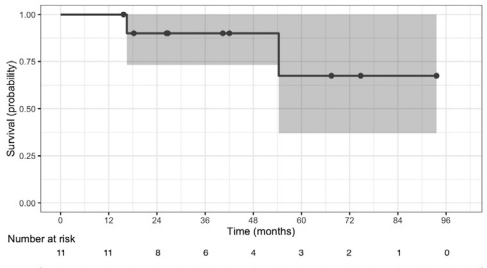

Figure 7. Kaplan-Meier survival analysis. Eleven patients determined to be outside the Milan criteria on explantation were analyzed for disease-specific survival after transplant. Dots denoted the time of censoring. Time 0 was the date of transplantation.

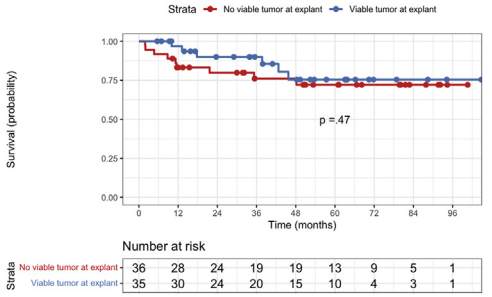

Figure 8. Kaplan-Meier survival analysis. Seventy-one patients who received transplantation were stratified by viable tumor in the explanted liver versus no residual tumor and were used to analyze postoperative overall survival. Dots denoted the time of censoring. Time 0 was the date of transplantation.

Table 4. Factors Affecting Survival

Factors	RFS		OS		DSS		WL DR	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
AFP	1.0 (1.0–1.0)	.05	1.0 (1.0–1.0)	.05	1.0 (1.0–1.0)	.51	1 (1.0–1.0)	.96
Microvascular invasion	0.6 (0.1–5.1)	.64	0.6 (0.1–5.2)	.66	2 (0.2–23)	.57		
Any evidence of LTP (pathology or imaging)	1 (0.3–3.1)	.99	0.9 (0.3–2.8)	.84	8.7 (0.8–99)	.08	0.7 (0.2–2.3)	.60
Tumor size	1.3 (0.7–2.4)	.36	1.3 (0.7–2.2)	.46	2.5 (1.2–5.2)	**.02***	0.9 (0.5–1.9)	.85

Note–Tumor size refers to the largest tumor at the first procedure, if multiple.
AFP = alpha-fetoprotein; CI = confidence interval; DSS = disease-specific survival; HR = hazard ratio; LTP = local tumor progression; RFS = recurrence-free survival; OS = overall survival; WL DR = waitlist dropout.
*Statistical significance.

of this study demonstrate excellent waitlist retention for patients bridged with MW ablation compared with that for historical controls (Table 5). No patients died while on the waitlist, and only 4.5% of patients dropped out because of development of multifocal HCC. There were no cases of tumor seeding or procedural adverse event resulting in waitlist removal. These findings support the use of MW in an "ablate and wait" strategy for both bridging and gaining knowledge about the natural history of tumors before transplant (7,11,22,23). The OS of patients who were successfully bridged and transplanted was high, with 1-, 3-, and 5-year rates of 97.2%, 85.1%, and 76.7%, respectively (and higher DSS), which compared favorably with other bridging studies (Table 5). Of the 15 transplanted patients who died, most deaths (n = 10) were due to non-HCC causes and, thus, unaffected by any bridging strategy.

An important question remains the choice of LRT, specifically ablation versus intra-arterial approaches. Many patients are better candidates for a specific LRT because of location, size of the tumor, local expertise, vascular anatomy, or condition; however, the choice is not clear for those who are candidates for both intra-arterial and ablation treatments. Most guidelines do not strongly recommend a specific LRT, and existing single-center trials have included patients bridged with both methods; however, the selection criteria are not randomized and may be biased (6,24,25). RF and TACE have been the most widely applied thermal and intra-arterial options for bridging, respectively, and both appear to decrease waitlist dropout (24,26–29). More recently, experience with Y-90 segmentectomy raises the possibility that transarterial radioembolization will become the intra-arterial bridging modality of choice (13,30–32). A recent large study (15) demonstrated a 45% rate of complete necrosis at explant, 77% OS at 5 years, and 11% HCC-specific mortality at 5 years after transplant (vs the current MW study, 80.5%, 76.7%, and 7.0%, respectively); however, the Y-90 study included more advanced stage patients. To date, there are no studies comparing Y-90 and MW ablation for bridging in patients who could receive either treatment.

A higher rate of complete necrosis at explant confers a survival advantage after transplant (10,11,27), and the 80.5% rate reported in this study is high compared with that in other methods of LRT. A total of 58 nonablated viable tumors were detected, and most were small (<1 cm), well differentiated, and without microvascular invasion. All patients found to be outside the Milan criteria by explant were from tumors too small to diagnose as HCC by imaging criteria, confirming the known limitations of pretransplant imaging (27). There was no correlation between a small-volume residual tumor at explant and survival after transplant. Likewise, there was no correlation between LTP

Table 5. Relevant Studies Reporting Locoregional Therapy as a Bridge to Transplantation

Study	Treatment method	No. of patients (n)	Waitlist time (mo)	LTP (%)	Posttransplant recurrence (%)	All-cause dropout (%)	HCC-specific dropout (%)	Overall survival (%)
Mazzaferro et al (2004) (36)	RF	50	9.5 (median)	N/A	3.3%	N/A	0%	83% (3-y)
Lu et al (2005) (29)	RF	52	12.7 (mean)	5.8%	0%	11.60%	5.8%	76% (3-y)
Millonig et al (2007) (37)	TACE	116	9 (median)	N/A	14.2%	8.60%	8.6%	N/A
Cillo et al (2007) (25)	RF, PEI (< Milan)	60	11.8 (median)	8.3%	0%	12.00%	N/A	69% (5-y)
	TACE (> Milan)	40	11.8 (median)	10%	0%	12.00%	N/A	79% (5-y)
DuBay et al (2011) (38)	RF	77 (RF) 93 (no treatment)	9.5 (median)	N/A	20%	34.00%	21%	N/A
Tohme et al (2013) (31)	Y-90	20	3.5 (median)	N/A	25%	N/A	N/A	79% (5-y)
Kluger et al (2014) (39)	TACE	225	11 (mean)	N/A	18%	11.10%	7.1%	74% (3-y)
	TAE	31	13 (mean)	N/A	12%	10%	3.2%	78% (3-y)
Sheth et al (2015) (2)	MW and RF	149 (procedures)	10.8 (median)	N/A	11%	N/A	7.2%	N/A
	TACE	66 (procedures)	10.8 (median)	N/A	11%	N/A	39%	N/A
Lee et al (2017) (26)	RF	121	10.2 (mean)	7.4%	5.6%	24.80%	7.4%	75.8 % (5-y)
Pommergaard et al (2018) (9)	RF	643	9.8 (median)	N/A	0.35 (HR)	N/A	N/A	80.9% (5-y)
	TACE	2110	9.8 (median)	N/A	0.78 (HR)	N/A	N/A	67.6% (5-y)
Affonso et al (2019) (40)	TACE	136	6.6 (mean)	N/A	5.8%	N/A	N/A	72% (5-y)
Zori et al (2020) (10)	Y-90	42	10.1 (mean)	N/A	10.7%	8.50%	1.1%	92.9% (3-y)
	TACE	52	8.6 (mean)	N/A	24.3%	13.80%	3.2%	75.7% (3-y)
Toskich et al (2021) (32)	Y-90	33	6.8 (median)	N/A	3%	0%	0%	N/A
Som et al (2021) (14)	MW	62	12.6 (median)	N/A	0%	N/A	N/A	87.1% (50 mo)
Couillard et al (current study)	MW	88	9.4 (median)	7.2%	7%	19.30%	4.5%	76.7% (5-y)

HCC = hepatocellular carcinoma; HR = hazard ratio; LTP = local tumor progression; MW = microwave; N/A = not applicable; RF = radiofrequency; TACE = transarterial chemoembolization; Y-90 = yttrium-90.

while waitlisted and posttransplant survival, likely because of the small volume of residual tumor and aggressive retreatment of radiologically detected recurrences. For example, in this study, 7 of 10 patients with LTP were rapidly retreated with LRT rather than observed, and 2 patients were promptly transplanted.

There are limited data comparing MW and RF for bridging; however, at several centers, there is a recent shift away from RF because of the known physical advantages of MW for tissue heating (2,33–35). Compared with a recent RF bridging study (25), local control with MW in this study was slightly higher (100% vs 91.7% technical success, 7.2% vs 7.4% LTP for MW and RF, respectively), and the rate of complete necrosis for targeted tumors was higher (80.5% vs 71.7%). Despite these potential advantages and increasing use, there is only one small study (29) of MW for bridging to transplant. Another recent description of MW in patients who received liver transplant demonstrated a lower rate of complete necrosis (66%) (14) but provided no information on waitlist dropout.

This study has several limitations. Only a single MW system was used, which may limit generalizability. The single-center, single-arm retrospective design is typical of bridging literature and of single-institution studies where there are expertise and bias toward a particular LRT (Table 5). At this study center, MW has been the thermal ablation modality of choice since 2010; therefore, there was no opportunity for comparison with RF or cryoablation. A multicenter, randomized controlled trial would be ideal for comparing LRT bridging methods but may never be performed given the need for large cohorts, long follow-up, and multiple centers.

The results of this study of MW as first-line LRT for bridging HCC patients to liver transplant demonstrated that MW ablation is a safe and effective bridging modality with high rates of disease-specific waitlist retention and posttransplant survival rivaling other LRT bridging strategies. Dropouts because of seeding or other complications were not encountered, and small pathologically detected HCC did not drive posttransplant survival. Although MW ablation appears to be an effective bridging strategy, this study did not compare MW ablation with intra-arterial therapies, external beam radiation, or other percutaneous ablation modalities, and future comparative studies are warranted.

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