Clinics in Oncology

Research Article
Published: 28 Sep, 2016

Hepatocellular Carcinoma - Review of Treatment Options with Percutaneous Ablative Therapies

*Jessica Goldman, Marc Solomon and Sohail Contractor**

Department of Radiology, New Jersey Medical School, USA

Abstract

Hepatocellular carcinoma is a cause of significant morbidity and mortality with many risk factors contributing to its development. The underlying risk factors have a geographic distribution with alcohol and hepatitis C being the predominant factors in the western world and hepatitis B in the eastern world. Diagnosis is based on classic imaging features on a contrast enhanced CT or MRI scan. Pathological features vary with some tumors displaying aggressive behavior with vascular invasion and metastatic disease. Treatment options for cure include surgical resection and transplantation depending upon underlying liver function. Non operative treatments have started to gain more acceptance with percutaneous thermal based ablative modalities, including radiofrequency and microwave ablation. Results of ablation are comparable to those of surgical resection, especially for smaller lesions. Other treatment options include transcatheter based embolic treatments and an oral multikinase inhibitor, Sorafenib.

Introduction

Hepatocellular Carcinoma (HCC) is the most common primary neoplasm of the liver. HCC is a significant cause of morbidity and mortality and carries an unfavorable prognosis with aggressive growth behavior and a high rate of recurrence [1,2]. HCC typically develops in the setting of chronic liver inflammation, such as infection with hepatitis B or C viruses [2]. Other risk factors for HCC are alcohol abuse, hereditary hemochromatosis, non-alcoholic fatty liver disease, stage 4 primary biliary cirrhosis, alpha 1 antitrypsin deficiency, and aflatoxin exposure [1]. Diabetes, which is associated with nonalcoholic fatty liver, is currently recognized as a risk factor for HCC as well [3]. The incidence of HCC has risen from 1.6 to 4.9 cases per 100,000 in the United States, most likely as a result of the growing number of cases of hepatitis C and Non-Alcoholic Steatohepatitis (NASH) [1,4]. Due to the endemicity of hepatitis B virus (HBV) in Asia, HCC is also prevalent in Asia [1].

Diagnostic Imaging for HCC

The increased incidence of HCC cases is due to both a real increase in disease occurrence as well as earlier diagnosis by modern imaging equipment [5]. Imaging techniques that are currently employed in the diagnosis, treatment planning, and management of HCC include ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI). The European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Disease recommend bi- annual US as the imaging modality of choice for the surveillance of patients at high risk of HCC.1Classically, on triphasic contrast-enhanced CT (CECT) or MRI, an HCC lesion exhibits intense arterial-phase enhancement followed by contrast washout in the delayed venous phase [6]. Findings such as heterogeneity, central necrosis, and abnormal internal vessels are associated with large HCC lesions [1].

Staging Systems for HCC

The Barcelona Clinic Liver Cancer (BCLC) staging system, which was initially proposed by Llovet et al. [7] in 1999, is considered the gold standard of staging systems for HCC. It is the only staging system that is endorsed by the AASLD and the EASL [8]. The BCLC system classifies HCC as very early, early, intermediate, or advanced [9]. Treatment strategies are correlated with the stage of the tumor [10]. Very early stage or stage 0 cancer is defined as a single nodule that is less than 2 cm and Child-Pugh class A. Early stage or stage A HCC is defined as a single nodule, or no more than 3 nodules, of 3 cm or less. Intermediate stage (stage B) and advanced stage (stage C) cancer represent multi nodular lesions and cases involving vascular invasion or extra hepatic spread, respectively. Terminal stage or stage D HCC corresponds to cases in which the patient has Child-

OPEN ACCESS

Correspondence:

Sohail Contractor, Department of Radiology, New Jersey Medical School, Rutgers NJMS, Newark, NJ, USA, Tel: 973-972-5188; Fax: 973-972-5997; E-mail: contrasg@njms.rutgers.edu

Received Date: *05 Sep 2016*

Accepted Date: *26 Sep 2016*

Published Date: *28 Sep 2016*

Citation:

Goldman J, Solomon M, Contractor S. Hepatocellular Carcinoma - Review of Treatment Options with Percutaneous Ablative Therapies. Clin Oncol. 2016; 1: 1107.

Table 1: The BCLC stage is influenced by the Child-Pugh score [12]. Five variables are evaluated, each of which is graded on a scale of 1 to 3. Child-Pugh A- score of 5-6 on above, Child-Pugh B- score of 7-9, Child-Pugh C score of 10-15.

Variable	1	2	3
Encephalopathy	None	Moderate	Severe
Ascites	None	Moderate	Severe
Bilirubin (mg/dl)	<2	3-Feb	>3
Albumin	>3.5	2.8-3.4	<2.8
Prothrombin time	<14	15-17	>18

Pugh class C cirrhosis or a performance status of 2 or greater. Resection and ablation or transplantation is recommended for stages 0 and A, transcatheter arterial chemoembolization (TACE) for stage B, sorafenib for stage C, and supportive care for stage D [9]. Sorafenib is a multikinase inhibitor with activity against Raf-1, B-Raf, vascular endothelial growth factor receptor 2, platelet-derived growth factor, and c-Kit receptors, among other kinases [11] (Table 1).

The Model for End-stage Liver Disease (MELD) system, which was initially developed to determine prognosis following a transjugular intra hepatic porto systemic shunt (TIPS) procedure for liver failure is now used to prioritize candidates for liver transplantation [12,13]. MELD score uses the serum Bilirubin, Sodium, INR, Creatinine and whether patient has had dialysis or CVVHD within week prior to the Creatinine measurement (Table 2).

The MELD score is calculated as follows:

MELD Score = 0.957 x log (creatinine [mg/dL]) + 0.378 x log (bilirubin [mg/dL]) + 1.12 x log (International Normalized Ratio [INR]) + 0.643 x (cause of cirrhosis [0 foralcohol-induced cirrhosis, 1 for non-alcohol induced cirrhosis) [14].

A higher score is associated with shorter survival. Patients with HCC are assigned a higher MELD score which places them higher on the list of patients waiting for a transplant [15]. The Conventional Milan Criteria (CMC), which were introduced to promote the attainment of positive outcomes in patients who meet them and avoid adverse

Out comes in those who do not, have improved results of orthotopic liver transplantation (OLT). Patients with a single HCC lesion below 5 cm or up to three lesions, each of which are below 3 cm, meet the CMC. Survival in these patients is 70% at 5 years, with a recurrence rate below 15% [10].

Therapeutic Options for HCC

Hepatic resection is considered the treatment of choice for HCC; however, at the time of diagnosis, less than 30 percent of cases are resectable [6]. Factors that preclude resection include extra hepatic metastases, vascular invasion, high-risk anatomical location, excessive size or number of lesions, inadequate functional liver to support life, and co- morbid conditions [16]. Patients with insufficient hepatic reserve due to underlying chronic liver disease with significant portal hypertension and abnormal bilirubin levels or multifocal distribution of tumor nodules are poor candidates for surgical resection. Interventional procedures such as percutaneous ethanol injection (PEI), thermal ablation, and TACE are options. Systemic chemotherapy, targeted molecular therapies, and radiation therapy are offered for select patients [17]. Only hepatectomy, liver transplantation, and percutaneous thermal ablation have curative potential. Sorafenib has been demonstrated to have prolonged overall survival rates when compared to placebo [1].

Table 2: The Cancer of the Liver Italian Program (CLIP) is an additional scoring system that has been used in the staging of HCC. This system uses the Child-Pugh score, tumor morphology, α-fetoprotein level and the presence or absence of portal vein thrombosis.

Variables		Scores	
	0	1	2
Child-Pugh	A	B	C
Tumor morphology	Uninodular and	Multinodular and	Massive or
	extension <=50%	extension <=50%	extension >50%
AFP (ng/dl)	<400	>=400	
Portal vein thrombosis	No	Yes	

These scores are added together to yield a CLIP score of 0-6, with median survival by CLIP score as follows: 0 = 42.5 months
1 = 32.0 months
2 = 16.5 months
3 = 4.5 months
4 = 2.5 months
5-6 = 1 month
The CLIP score has been found to be a good predictor of survival recurrence [15].

Ablative Therapies

Ablative therapies deliver chemicals or thermal energy directly to tumors to induce necrosis [1]. Tumor ablation began in the 1980s with the use of PEI. Although PEI produced survival rates nearly equal to those of surgical resection for small HCC lesions, multiple treatment sessions, sometimes as many as five, were necessary to achieve complete ablation [3]. Additionally, PEI is occasionally ineffective in the setting of intra- or extra- capsular invasion due to hindered diffusion of ethanol in fibrotic tissues. As nodule size increases, the effectiveness of PEI rapidly decreases [18].

Thermal ablation employs delivery of targeted energy to achieve tumor necrosis. Radiofrequency ablation (RFA) was one of the earliest of these technologies. Because of its ability to achieve complete ablation in fewer sessions than PEI, with survival data equivalent to that of PEI, RFA gained popularity and quickly became the treatment of choice for HCC. Recently conducted meta-analyses of randomized controlled trials comparing RFA to PEI have shown RFA to have a slight survival advantage over PEI. However, recent development of multi-tined ethanol infusion needles have augmented the effectiveness of single-session ethanol instillations, which, in combination with the lower cost of PEI, has resulted in its preferred use over RFA, particularly in poorer regions [3].

In RFA, an electrical current in the radiofrequency range of the electromagnetic spectrum is applied through a needle electrode, either surgically or under image guidance, producing heat-based thermal cytotoxicity [1]. The electrical circuit is completed through the body with current exiting through grounding pads, which are dispersing electrodes attached to the thighs or back that cover a large surface area.

Dispersion of current over the surface area encompassed by the grounding pads prevents burns at the exit site, while current density in close proximity to the needle electrode permits attainment of temperatures in the 60-100°C range that are conducive to almost instantaneous coagulative necrosis. However, tumor ablation with

a single-needle electrode is generally not consistent as the resultant zone of necrosis is usually marginal. With the advent of expandable electrodes inserted via a single needle, internally cooled electrodes, cluster electrodes, and saline instillation via the electrode, larger ablation zones are achieved, enabling RFA of tumors in the 2-5 cm range [3]. A margin of 0.5-1 cm of viable liver tissue is typically targeted to ensure treatment of the peripheral tumor as well as any microscopic extensions beyond the radio graphically visible confines [1].

The technical success of heat-based ablation is more appreciable in RFA of HCC lesions than in ablation of liver metastases due to the so-called "oven effect." Both the underlying cirrhotic liver in patients with HCC, and the tumor's surrounding capsule serve as thermal insulators. Consequently, higher peak temperatures are achieved. Another phenomenon associated with RFA is the so-called "heat-sink effect," which refers to the cooling of tumors adjacent to large vessels secondary to continuous inflow of blood at body temperature. Peak temperatures achieved in tumors next to blood vessels are cooler than desired and cytotoxic temperatures may not persist for a sufficient duration resulting in zones of ablation with areas of viable tumor near the vessel. While often described in association with such large vessels as the Inferior Vena Cava (IVC) and hepatic veins, this effect can be observed in the setting of vessels as small as 4 mm [3].

Absolute contraindications to RFA are severe bleeding diathesis (platelet count below 50,000/μL), hemodynamic instability, large as cites, jaundice, and presence of metallic devices such as pacemakers. Relative contraindications to RFA are lesions situated close to the gastrointestinal tract, biliary system, and heart. RFA is also not advised for tumors located within 1 cm of the hepatic portal tract [1]. HCC lesions located near the hepatic hilum or gallbladder have the risk of thermal injury to the biliary system or gallbladder with resultant leaks or strictures. Treatment of subcapsular or exophytic lesions may be complicated by thermal injury to adjacent gastrointestinal organs, the abdominal wall, or diaphragm. Intra-peritoneal bleeding or tumor seeding may ensue [19]. Major complications, include hepatic failure, hemorrhage, infection, abscesses, intercostal nerve injury, organ injury, tumor lysis syndrome, and pneumothorax [1].

Microwave ablation (MWA) has been recently gaining ground as a viable ablative therapy for several reasons. While RFA is executed using alternating currents in the 400-500 kHz frequency range, MWA employs non-ionizing electromagnetic fields in the 1 GHz frequency range. MWA was first performed clinically in the 1980's and 90's, control over the emitted field was limited and ablation of large tumors required a high amount of power, resulting in subpar coagulative necrosis and a relatively high rate of complications [20]. Until these limitations were addressed, RFA remained the gold standard for ablation [18]. Where as RFA was developed in Western countries in the early 90's, MWA was developed in Oriental countries and has only recently gained popularity in Western countries [21].

Physical differences between RFA and MWA account for the advantages of MWA over RFA. RFA is dependent on ohmic dissipation effects associated with the circulation of alternating electric currents within target tissues and is dependent on passive conduction of heat, i.e., each heated tissue molecule heats the adjacent tissue molecule, leading to loss of energy as the distance from the probe increases. At temperatures that exceed °C, dehydration100 and subsequent carbonization of tissues may occur, impeding further radiofrequency (RF) heating. This upper temperature limit efficacy in the active heating zone, i.e., the inner treatment region in which heating is mostly due to absorption and dissipation of the energy delivered by the ablation probe, disrupts indirect peripheral heating, i.e., the passive transfer of heat from the active zone outwards via thermal conduction. As a result, the coagulative performance of a single probe is limited, tissues with low electrical conductivity respond poorly, and susceptibility to heat-sinking effects is typical in RFA [18].

Microwave ablation utilizes a dielectric heating modality with propagation of electromagnetic radiation through a biologic tissue inducing a fast switching rotation of electric dipoles at an atomic or molecular level. Microscopic charge displacement, without the generation of macroscopic electric current, is countered by inter dipolar interactions, leading to the production of frictional heat. Polar molecules such as water are particularly responsive to the dielectric heating mechanism. The implication of this is that tissues with high water content are susceptible to heating by microwaves (MWs), while tissues with a low water content, which would hamper the circulation of RF currents, absorb a smaller proportion of the delivered MW field energy, enabling extension to the next tissue layer. Tissue carbonization thus does not hinder the MW heating process, °C meaning maybe reached that temperatures much greater than 100 within the target lesion, augmenting active and passive tissue heating, producing larger zones of coagulation, and minimizing heat-sinking effects [18].

In contrast to RFA, MWA does not require the completion of an electrical circuit through the patient. Grounding pads, therefore, are not necessary in MWA, avoiding the risk of skin burns at the site of the pads [3]. Furthermore, metallic materials such as surgical clips and pacemakers are not considered a contraindication to MWA therapy [1]. Another advantage to MW systems is that multiple antennas can be powered simultaneously, allowing for the production of larger volumes of necrosis. MW ablated areas are also less susceptible to the heat sink effects than RFA treated areas allowing for better treatment zones adjacent to vessels [3].

MW systems in the United States are available in frequencies of 915 MHz or 2.54 GHz [3]. The components of MW systems include a generator, a monopolar electrode, and a coaxial cable that connects the electrode to the generator [1]. Until recently, the clinical MW systems in the United States and Europe were limited by antenna shaft heating from reflected power, large antenna diameters, and low power output producing ablation zones of small diameter. Modern-day MW systems circumvent the reflection of heat along the cable needle shaft by circulating fluid internally through the needle shaft, thereby preventing skin burns at the insertion site [22]. Innovative MWA probes employ gas such as carbon dioxide to cool the shaft [3]. An advantage that MWA has over RFA is the ability to treat multiple lesions with multiple electrodes. In particular, each MW application is capable of producing a discrete focus of approximately 1.6 cm of necrosis for 120 s at 60 W [1]. Preclinical studies have shown that ablation times are faster with MWA than with RFA [3]. Additionally, tissue boiling and charring, which increase impedance and diminish electrical and thermal conductivity, limit the effect of RFA but not that of MWA [1].

With earlier MWA technologies, the radiated field pattern was difficult to predict. In addition, uncontrolled back-heating effects were frequent. This so-called "comet effect" was due to impedance mismatches between the antenna and target tissues, resulting in back-propagation of MW radiations not absorbed by target tissues

Table 3: Key Differences between RFA and MWA.

	RFA	MWA
Energy source	Electric current	Electromagnetic radiation
Grounding pads	Yes	No
Tissue carbonization	May occur	Does not occur
Intratumoral temperatures	Lower	Higher
Ablation zone	Smaller	Larger
Procedural time	Longer	Shorter
Number of lesions per	Single	Multiple
treatment session		
Tumor size	Best outcomes with tumors	Ablation possible with
	below 4 cm in diameter	tumors 5-8 cm
Heat-sink effect	Yes	No
Metallic devices	Contraindicated	Not contraindicated

along the outer walls of the probe shaft. Consequently, undesired deep cauterization of tissues along the probe shaft would occur and increase the risk of complications. Furthermore, because of reduced antenna efficiency, the MW field would be dispersed longitudinally rather than focused on the distal end of the probe. Newer MWA probe designs have resolved these issues, permitting the safe delivery of large, spherical, and controllable ablations. Monopole or dipole antennas with an impedance transformer superimposed on the coaxial antenna, know as a miniaturized choke, trap reflected waves through a destructive interference pattern. Triaxial antennas are able to absorb reflected waves owing to encompassment of the main coaxial line by an outer coaxial line [18].

MWA is similar to RFA with respect to its indications and contraindications. An important advantage of MWA, however, is the ability to ablate 5-8 cm tumors [1]. Although no precise tumor size beyond which RFA should be applied has been established, the best outcomes are achieved with tumors below 4 cm in diameter [17]. Major complications associated with MWA include bile duct stenosis, bleeding, hemothorax, intrahepatic hematoma, peritoneal hemorrhage, hepatic abscess, colonic perforation, and tumor seeding. Minor complications include pain, asymptomatic pleural effusions, and post-ablation syndrome [1]. Post-ablation syndrome describes a constellation of symptoms comprising fever, malaise, nausea, vomiting, and pain at the site of ablation. It tends to develop in the setting of larger ablation volumes or the treatment of multiple tumors in a single session. Treatment is usually supportive, with resolution typically occurring over the span of a few days. Symptoms that persist beyond seven days should raise suspicion for more ominous complications such as infection or biliary injury [19] (Table 3) summarizes the key differences between RFA and MWA.

Outcomes in RFA versus MWA

A number of studies have been conducted to determine which ablative method, between RFA and MWA, is superior. Zhang et al. [6], who compared the therapeutic efficacy of RFA versus MWA for HCC lesions measuring 5 cm or less, found no significant differences in Complete Ablation (CA), Local Tumor Progression (LTP), distant recurrence (DR), complication rates, and overall survival. In their study, CA was defined as uniform low attenuation on CT without enhancement in the ablation zone with a diameter exceeding that of the treated tumor. Incomplete ablation (IA) referred to any irregular contrast enhancement found inside or beside the ablation zone. While LTP was defined as the appearance of tumor enhancement inside or adjacent to the ablated lesion, DR was defined as the new presence of intra hepatic HCC. Lu et al. [4], who studied a group of 102 patients with HCC, found no difference in local tumor control between RFA and MWA [6].

Reyad et al. [17] also compared the therapeutic efficacy of MWA to that of RFA for HCC lesions measuring up to 5 cm in greatest diameter. Although no significant difference in CA was found between MWA and RFA for tumors of 3 cm or less, for tumors 3.1-≤ 5 cm in diameter, CA was higher in the MWA group than in the RFA group. Partial ablation (PA), which was analogous to Zhang et al. [6] IA, was not significantly different between RFA and MWA in tumors less than 3 cm. However, PA was significantly lower in MWA than in RFA for tumors 3.1-≤ 5 cm in diameter. Reyad et al. [17] consequently deduced that MWA was more effective than RFA, especially for large tumors 3.1-≤ 5 cm in diameter, and that the time needed to achieve CA is significantly shorter for MWA than for RFA. While no significant difference was found in LTP between MWA and RFA for tumors of 3 cm or less, LTP was significantly higher after RFA than after MWA in larger tumors 3.1-≤ 5 cm in diameter. DR was not significantly different between MWA and RF A [17].

Zhang et al. [6] evaluated laboratory variables and discovered that AST and ALT levels were significantly elevated 48 hours after both RFA and MWA. However, the increase in AST and ALT levels was significantly larger after MWA than after RFA. One explanation that may account for this difference is the higher treatment temperatures and larger ablation zones possible with MWA. With regard to complications, post-procedural pain was significantly more frequent after MWA than after RFA, which may be due to the higher power outputs and larger ablation zones with the cooled-shaft antenna in MWA. Lu et al. [4] found that, for tumors 3.1-5.0 cm in diameter, disease-free survival was significantly better with RFA than with MWA. This difference may be attributable to the number of tumors ablated in the MWA group as compared to the RFA group. Multiple nodules are a significant independent factor for recurrence-free survival of the disease [6].

Laboratory variables and complications after RFA and MWA were also compared by Reyad et al. [17]. They found that AST and ALT levels were significantly higher 72 hours after both RFA and MWA, with a significantly higher increase after MWA than after RFA. The most common minor complications they observed were post-procedural pain, fever, and asymptomatic pleural effusion, with no significant difference between RFA and MWA. No significant difference in the proportion of patients who experienced major complications was found between the RFA and MWA groups. Reyad et al. [17] findings are in partial discordance with those of Zhang et al. [6], all of whom found no significant difference in CA, LTP, DR, and complications between RFA and MWA. Regarding AST and ALT levels, the findings of Reyad et al. [17] are in accordance with those of [6,17] concluded that both RFA and MWA are relatively safe procedures but with significantly different complication rates [17].

Vogl et al. [5], retrospectively evaluated and compared the therapeutic response of HCC to RFA and MWA, found no significant difference in complete therapeutic response rates, residual foci of untreated disease, recurrence rates after 3, 6, 9, and 12 months, and survival rates at 1, 2, and 3 years [5,23], who systematically reviewed the complications of RFA and MWA, found no statistically

significant difference in mortality rates, major complications, and minor complications between the two groups. They noted that the most common major complications were intra peritoneal, sub capsular, pleural, biliary, and retroperitoneal hemorrhage requiring blood transfusion. Other major complications included portal vein thrombosis, intra-hepatic hematoma, bile leak, biloma, bile duct injury, liver dysfunction, liver abscess, intestinal perforation, diaphragmatic hernia, hemothorax, intractable pleural effusion, and tumor implantation. Such complications as liver failure, intra peritoneal hemorrhage, bile duct injury, and tumor seeding are serious and life-threatening, whereas other complications can prolong hospitalization and increase morbidity. Lahat et al. [23] concluded that both RFA and MWA can be considered safe techniques for the treatment of hepatic tumors.

Abdelaziz et al. [12] studied the safety and efficacy of RFA and MWA in the ablation of early stage HCC lesions. They found no significant difference in CA between RFA and MWA, even after sub-classifying ≤3 cm lesionsand3 into -5 cm. These results are consistent with those of Lu et al. [4] who compared ≤3 the two ablative techniques for lesions cm and those greater than 3 cm. Procedure-related complications, which included sub capsular hematoma, thigh burn, abdominal wall skin burn, and pleural effusion, were not significantly different between RFA and MWA. Follow-up of both groups, however, revealed a significantly lower incidence of local recurrence in the MWA group as compared to the RFA group. With respect to the development of de novo lesions, portal vein thrombosis, and abdominal lymphadenopathy, no significant difference was found between the two groups. Overall survival at 1 and 2 years was not significantly different between the RFA and MWA groups. Abdelaziz et al. [12] concluded that both RFA and MWA lead to safe and equivalent ablation and survival rates and that MWA is superior to RFA in regard to local recurrence. For patients who are poor candidates for surgical resection, both ablative techniques are good alternatives.

Lu et al. [4] found no significant difference in local recurrence between RFA and MWA. Additionally, they found both groups to be equivalent in terms of complications and long- term survival. In a retrospective study by Ohmoto et al., RFA was found to be more effective in the treatment of small HCC lesions than MWA, with a lower rate of local recurrence and a higher survival rate. More recent studies in which newer MW systems were employed have proven MWA efficacious. In particular, Qian et al. [6] compared the performance of MWA using a cooled-shaft antenna to that of RFA using a cooled electrode in *in vivo* porcine liver tissues as well as in patients with small HCC lesions ranging in diameter from 1.2-3.0 cm. In an *in vivo* animal study, they found that MWA produced a significantly greater ablation volume compared to RFA. Furthermore, all three axes of the ablation volume produced by MWA were greater than those of RFA, demonstrating that technological advancements in MWA devices result in more spherical ablation areas [18].

Di Vece et al. compared the ablation area produced by a single application of MWA to that produced by an internally cooled RFA system in 40 patients with both primary and secondary inoperable liver tumors and found the long- and short- axis diameters of the ablation areas produced by MWA to be significantly greater than those produced by RFA. Clinical trials with new generation MWA devices seem to prove that MWA produces larger ablation volumes than RFA, with faster ablation times. Improvements in MWA devices are also enabling the performance of percutaneous thermal ablation on medium and large HCC lesions. Yin et al. who treated 109 patients with HCC lesions measuring 3.0-7.0 cm with percutaneous RFA or MWA, found no significant difference in CA rates between RFA and MWA [18].

Results regarding local disease control rates with MWA as compared to RFA are controversial. Early reports show comparable rates for local tumor control after MWA and RFA. A majority of published studies support the comparability of the two techniques in overall survival, local recurrence, and complication rates. Ding et al. however, found fewer recurrences after RFA than after MWA. They attribute this difference to the size of the lesions ablated, noting that a greater proportion of lesions in the MWA group exceeded 3 cm relative to the RFA group. Lesion size is known to influence local recurrence and it appears to have affected these results. Across studies, survival rates after MWA and RFA are generally comparable [1]. A prospective multi- institutional trial with variable clinical validation models would be beneficial [17].

Conclusion

HCC is a major cause of morbidity and mortality worldwide. It is a malignant neoplasm with a poor prognosis. HCC is being detected earlier and at increasing rates, due to both higher disease incidence and available imaging techniques. Management is based on the stage of disease. Current curative treatments include hepatic resection, liver transplantation, and percutaneous thermal ablation. Evolution of ablative techniques from PEI to RFA and now MWA continues to provide improved local tumor control as well as overall survival.

References

1. Poulou LS, Botsa E, Thanou I, Ziakas PD, Thanos L. Percutaneous microwave ablationvs radiofrequency ablation in the treatment of hepatocellular carcinoma. World J Hepatol. 2015; 7: 1054-1063.
2. Hetta OM, Shebrya NH, Amin SK. Ultrasound-guided microwave ablation of hepatocellular carcinoma: Initial institutional experience. Egy J Radiol Nucl Med. 2011; 42: 343-349.
3. Gervais DA, Arellano RS. Percutaneous tumor ablation for hepatocellular carcinoma. Am J Roentgenol. 2011; 197: 789-794.
4. Yu NC, Lu DS, Raman SS, Dupuy DE, Simon CJ, Lassman C, et al. Hepatocellular carcinoma: microwave ablation with multiple straight and loop antenna clusters-pilot comparison with pathologic findings. Radiology. 2006; 239: 269-275.
5. Vogl TJ, Farshid P, Naguib NN, Zangos S, Bodelle B, Paul J, et al. Ablation therapy of hepatocellular carcinoma: a comparative study between radiofrequency and microwave ablation. Abdom Imaging. 2015; 40:1829-1837.
6. Zhang L, Wang N, Shen Q, Cheng W, Qian GJ. Therapeutic efficacy of percutaneous radiofrequency ablation versus microwave ablation for hepatocellular carcinoma. PLoS One. 2013; 8: e76119.
7. Yi PS, Zhang M, Zhao JT, Xu MQ. Liver resection for intermediate hepatocellular carcinoma. World J Hepatol. 2016; 8: 607-615.
8. Zhong JH, Rodriguez AC, Ke Y, Wang YY, Wang L, Li Q. Hepatic resection as a safe and effective treatment for hepatocellular carcinoma involving a single large tumor, multiple tumors, or macrovascular invasion. Medicine (Baltimore). 2015; 94: e396.
9. Kudo M. Clinical practice guidelines for hepatocellular carcinoma differ between Japan, United States, and Europe. Liver Cancer. 2015; 4: 85-95.
10. Delis SG, Dervenis C. Selection criteria for liver resection in patients with hepatocellular carcinoma and chronic liver disease. World J Gastroenterol. 2008; 14: 3452-3460.

11. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. Hepatology. 2011; 53: 1020-1022.

12. 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 experiences. Surg Endosc. 2014; 28: 3429-3434.

13. Subramaniam S, Kelley RK, Venook AP. A review of hepatocellular carcinoma (HCC) staging systems. Chin Clin Oncol. 2013; 2: 33.

14. Brown DB, Nikolic B, Covey AM, Nutting CW, Saad WE, Salem R, et al. Quality improvement guidelines for transhepatic arterial chemoembolization, embolization, and chemotherapeutic infusion for hepatic malignancy. J Vas Interv Radiol. 2012; 23: 287-294.

15. Parikh S, Hyman D. Hepatocellular cancer: a guide for the internist. Am J Med. 2007; 120: 194-202.

16. Xu Q, Kobayashi S, Ye X, Meng X. Comparison of hepatic resection and radiofrequency ablation for small hepatocellular carcinoma: a meta-analysis of 16,103 patients. Sci Rep. 2014; 4: 7252.

17. Reyad M, El-Sawy A, El-Badry AM, Mahmoud L. Microwave ablation versus radiofrequency ablation for hepatocellular carcinoma: Effectiveness and prognosis. Global Advanced Research Journal of Medicine and Medical Sciences. 2016; 5: 67-73.

18. Poggi G, Tosoratti N, Montagna B, Picchi C. Microwave ablation of hepatocellular carcinoma. World J Hepatol. 2015; 7: 2578-2589.

19. Martinez-Camacho A, Laskey H, Cook B. Radiofrequency ablation for the local treatment of hepatocellular carcinoma. Cancer Research Frontiers. 2015; 1: 225.

20. Liang P, Yu X, Yu J. Microwave ablation treatment of solid tumors. Dordrecht: Springer Science + Business Media. 2015; 17-28.

21. Poggi G, Montagna B, DI Cesare P, Riva G, Bernardo G, Mazzucco M, et al. Microwave ablation of hepatocellular carcinoma using a new percutaneous device: preliminary results. Anticancer Res. 2013; 33: 1221-1227.

22. Ziemlewicz TJ, Hinshaw JL, Lubner MG, Brace CL, Alexander ML, Agarwal P, et al. Percutaneous microwave ablation of hepatocellular carcinoma with a gas-cooledsystem: initial clinical results with 107 tumors. J Vasc Interv Radiol. 2015; 26: 62-68.

23. Lahat E, Eshkenazy R, Zendel A, Bar Zakai B, Maor M, Dreznik Y, et al. Complications after percutaneous ablation of liver tumors: a systematic revew. Hepatobiliary Surg Nutr. 2014; 3: 317-323.