LABORATORY INVESTIGATION

Combination Therapies: Quantifying the Effects of Transarterial Embolization on Microwave Ablation Zones

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ABSTRACT

Purpose: To quantify the effect of transarterial embolization on microwave (MW) ablations in an in vivo porcine liver model.

Materials and Methods: Hepatic arteriography and cone-beam computed tomography (CT) scans were performed in 6 female domestic swine. Two lobes were embolized to an endpoint of substasis with 100–300-μm microspheres. MW ablations (65 W, 5 min) were created in embolized (n = 15) and nonembolized (n = 12) liver by using a 2.45-GHz system and single antenna. Cone-beam CT scans were obtained to monitor the ablations, document gas formation, and characterize arterial flow. Ablation zones were excised and sectioned. A mixed-effects model was used to compare ablation zone diameter, length, area, and circularity.

Results: Combined transarterial embolization and MW ablation zones had significantly greater area (mean ± standard deviation, 11.8 cm^2 ± 2.5), length (4.8 cm ± 0.5), and diameter (3.1 cm ± 0.6) compared with MW only (7.1 cm^2 ± 1.9, 3.7 cm ± 0.6, and 2.4 cm ± 0.3, respectively; $P = .0085$, $P = .0077$, and $P = .0267$, respectively). Ablation zone circularity was similar between groups ($P = .9291$). The larger size of the combined ablation zones was predominantly the result of an increase in size of the peripheral noncharred zone of coagulation (1.3 cm ± 0.4 vs 0.8 cm ± 0.2; $P = .0104$). Cone-beam CT scans demonstrated greater gas formation during combined ablations (1.8 cm vs 1.1 cm, respectively). Mean maximum temperatures 1 cm from the MW antennas were 86.6°C and 68.7°C for the combined embolization/ablation and MW-only groups, respectively.

Conclusions: Combining transarterial embolization and MW ablation increased ablation zone diameter and area by approximately 27% and 66%, respectively, in an in vivo non–tumor-bearing porcine liver model. This is largely the result of an increase in the size of the peripheral ablation zone, which is most susceptible to local blood flow.

ABBREVIATIONS

HCC = hepatocellular carcinoma, MW = microwave, OS = overall survival, RF = radiofrequency

Thermal ablation and transarterial embolization or chemoembolization are effective techniques to achieve local control of a variety of tumors, including hepatocellular carcinoma (HCC) (1–4). Although each is effective as monotherapy, there is increasing interest in combining transarterial embolization and ablation for the treatment of large, poorly visualized, or infiltrative HCC, as recent studies (5–9) have demonstrated improved oncologic outcomes compared with either therapy alone.

Most studies of combined embolization and ablation have involved radiofrequency (RF) ablation, long considered the clinical standard ablative modality for HCC. Larger treatment volumes have been achieved when RF ablation was combined with transarterial embolization or chemoembolization (vs RF

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EDITORS' RESEARCH HIGHLIGHTS

- Transarterial embolization with microwave (MW) ablation resulted in larger ablation zones compared with MW ablation alone, with observed ablation zones even larger than dimensions provided in the device instructions for use.
- The increased ablation zone was caused by expansion of the peripheral zone of ablation, the area most susceptible to heat-sink effects, presumably by decreasing heat loss from hepatic arterial branches.
- Embolization before MW ablation resulted in higher temperatures and faster temperature elevation 1 cm from the MW antenna.

ablation alone) in animal models (10–12). Several retrospective clinical studies (7,8) have also demonstrated improved overall survival (OS), improved recurrence-free survival, and decreased rate of disease progression with combination therapy (ie, chemoembolization with RF ablation) compared with RF ablation alone for the treatment of HCC.

Microwave (MW) ablation is increasingly used in lieu of RF ablation, and it has been associated with improved oncologic outcomes (including lower rates of local tumor progression) and an ability to more effectively treat larger tumors compared with RF ablation monotherapy (3,4,13). Fewer studies have evaluated the effectiveness of combining chemoembolization with MW ablation, but the existing studies have demonstrated favorable results, with improvements in OS (14). Although these studies are important to demonstrate clinical outcomes, there are few data to guide clinicians on the anticipated change in ablation zone size or shape when MW ablation is combined with transarterial embolization.

Successful interventional oncologic treatments require careful preprocedural planning and a thorough understanding of the tissue response to various treatment modalities and parameters. Quantifying the effect of transarterial embolization before ablation will facilitate more accurate prediction of posttreatment ablation zone size, shape, and reproducibility (12). This is particularly important given that under- or overtreatment of tumors can have deleterious effects. An assumption that the embolization will augment the ablation more than it does may lead to an incomplete treatment and residual viable tumor (15,16). An underestimation of the increase in size of the MW ablation zone after embolization may lead to unintended thermal injury to adjacent critical structures, such as a central bile duct or bowel (4,17–19). Therefore, the purpose of the present study is to quantify the effect of embolization on MW ablation zone size, shape, and reproducibility in an in vivo porcine liver model.

MATERIALS AND METHODS

In Vivo Techniques

All studies were performed with approval from the institutional animal care and use committee and complied with National Research Council guidelines (20). Female domestic swine (n = 6; approximate weight, 50 kg; approximate age, 3–4 mo; Arlington Farms, Arlington, Wisconsin) were sedated with intramuscular tiletamine hydrochloride/zolazepam hydrochloride (7 mg/kg; Telazol; Fort Dodge Animal Health, Fort Dodge, Iowa) and xylazine hydrochloride (2.2 mg/kg; Xyla-Ject; Phoenix, St. Joseph, Missouri). Anesthesia was maintained with inhaled 1.0%–2.0% isoflurane (Halocarbon, River Edge, New Jersey). An auricular vein was cannulated with a 20-gauge angiocatheter for administration of intravenous fluids. A cutdown was performed on the right common femoral artery, and a midline incision was used to surgically expose the liver of each animal to facilitate optimal antenna placement into the liver lobes.

Transarterial Embolization

After the right common femoral artery was exposed surgically, the artery was directly punctured with an 18-gauge needle. A 5-F vascular sheath was placed. An aortogram was obtained to identify the hepatic arterial anatomy. A 4-F angled Glide catheter was used to select the common hepatic artery. Digital subtraction arteriograms were obtained to delineate the hepatic arterial branches (**Fig 1a**). Cone-beam CT scans were obtained with the catheter in the common hepatic artery to further characterize hepatic arterial anatomy and identify individual branches supplying each of the four liver lobes. Two of the four liver lobes (right medial and lateral or left medial and lateral) were subsequently embolized under fluoroscopic guidance to an endpoint of stasis for 5 heartbeats with the use of 100–300-μm Embosphere Microspheres (Merit Medical, South Jordan, Utah). The embolized lobes were altered to minimize any bias or effect particular lobes might have on the ablation zones. The embolizations were performed by using the 4-F angled Glide catheter or a 2.8-F microcatheter (Progreat; Terumo, Tokyo, Japan) depending on the size of the target branch. Postembolization arteriograms and cone-beam CT scans were obtained to confirm adequate embolization of the target lobes (**Fig 1b**).

MW Ablation

MW ablations were performed immediately following embolization by using a 2.45-GHz system and single 17-gauge antenna (Certus 140 and PR-15; NeuWave Medical, Madison, Wisconsin) in embolized (n = 15 total ablations) and nonembolized (n = 12 total ablations) lobes of the liver. One ablation was performed per liver lobe with the exception of a single embolized lobe that was large enough to accommodate two ablations. In that lobe, the first ablation was performed in a peripheral location to minimize its effect on the perfusion at the location of the second ablation. The open porcine abdomen allowed probes to be placed directly into the liver. The position of the antenna was manually palpated to ensure that the antenna was centered within the desired lobe. The ablations were performed one at a time. After they had been placed, the antennas were secured into