Percutaneous Ablation of Peribiliary Tumors with Irreversible Electroporation

Mikhail T. Silk, BS, Thomas Wimmer, MD, Kyungmouk S. Lee, MD, Govindarajan Srimathveeravalli, PhD, Karren T. Brown, MD, Peter T. Kingham, MD, Yuman Fong, MD, Jeremy C. Durack, MD, Constantinos T. Sofocleous, MD, and Stephen B. Solomon, MD

ABSTRACT

Purpose: To assess biliary complications after irreversible electroporation (IRE) ablation of hepatic tumors located < 1 cm from major bile ducts.

Materials and Methods: A retrospective review was conducted of all percutaneous IRE ablations of hepatic tumors within 1 cm of the common, left, or right hepatic ducts at a single institution from January 2011 to September 2012. Computed tomography imaging performed before and after treatment was examined for evidence of bile duct dilatation, stricture, or leakage. Serum bilirubin and alkaline phosphatase levels were analyzed for evidence of biliary injury.

Results: There were 22 hepatic metastases in 11 patients with at least one tumor within 1 cm of the common, left, or right hepatic duct that were treated with IRE ablations in 15 sessions. Median tumor size treated was 3.0 cm (mean, 2.8 cm ± 1.2, range, 1.0–4.7 cm). Laboratory values obtained after IRE were considered abnormal after four treatment sessions in three patients (bilirubin, 2.6–17.6 mg/dL; alkaline phosphatase, 130–1,035 U/L); these abnormal values were transient in two sessions. Two patients had prolonged elevation of values, and one required stent placement; both of these conditions appeared to be secondary to tumor progression rather than bile duct injury.

Conclusions: This clinical experience suggests that IRE may be a treatment option for centrally located liver tumors with margins adjacent to major bile ducts where thermal ablation techniques are contraindicated. Further studies with extended follow-up periods are necessary to establish the safety profile of IRE in this setting.

ABBREVIATION

IRE = irreversible electroporation

Nearly 70% of hepatic metastases are unresectable because of anatomic location, limited functional liver reserve, or comorbidities (1,2). Without treatment, the 5-year survival for metastatic liver disease is < 1% (3). Percutaneous thermal ablation techniques have been shown to be an effective tool for treating tumors, increasing 5-year survival of hepatocellular carcinoma to 33%–54% and colorectal metastasis to 25%–46% (4). However, a large population remains ineligible for thermal techniques because of tumor proximity to main biliary tracts (5).

Irreversible electroporation (IRE) is a nonthermal ablation technique that uses pulsed direct current to induce cell death (6). Although cell death is believed to occur via the formation of permanent nanopores in the cell membrane, the extracellular matrix appears to remain intact (7). It is hypothesized that although tumor cells near bile ducts treated with IRE may die, bile ducts in the ablation zone may retain their structural integrity secondary to intact extracellular matrix. Additionally, the efficacy of IRE is not limited by heat sink effects (8,9). Previous clinical studies suggested the safety and efficacy of IRE in the liver and pancreas. Thomson et al (10) investigated the safety of IRE in humans including hepatic ablations. Narayanan et al

From the Interventional Radiology Service (M.T.S., T.W., K.S.L., G.D., K.T.B., J.C.D., C.T.S., S.B.S.), Department of Radiology, and Department of Surgery (P.T.K., Y.F.), Memorial Sloan-Kettering Cancer Center, 444 East 68th Street, New York, NY 10065; and Department of Radiology (T.W.), Medical University of Graz, Graz, Austria. Received April 22, 2013; final revision received and accepted October 11, 2013. **Address correspondence to** M.T.S.; E-mail: Mikhail.Silk@gmail.com

S.B.S. received an unrestricted grant and equipment from AngioDynamics and is a consultant for Covidien and Johnson&Johnson. None of the other authors have identified a conflict of interest.

J Vasc Interv Radiol 2014; 25:112–118

http://dx.doi.org/10.1016/j.jvir.2013.10.012

(11) reported on the clinical safety of IRE in the pancreas, a target organ where the structural integrity of blood vessels and biliary ducts needs to be maintained after ablation. Two reports have discussed peribiliary IRE ablations. Kingham et al (12) studied the effects of IRE on hepatic veins and the portal pedicle but included smaller tumors with a median size of 1 cm. Although this study was primarily focused on the effects of IRE ablation on hepatic blood vessels, effects on the biliary ducts and liver function were also evaluated. Cannon et al (13) examined the general safety of centrally located hepatic IRE ablations.

The purpose of this clinical study was to examine specifically the safety of IRE for larger, more centrally located liver tumors with tumor margins in close proximity to major bile ducts where thermal techniques are contraindicated. We assessed possible complications and the safety of IRE ablation for hepatic tumors located within 1 cm of the common, left, or right hepatic ducts. We retrospectively examined serum bilirubin, alkaline phosphatase, and computed tomography (CT) imaging studies for evidence of bile duct dilatation or leakage.

MATERIALS AND METHODS

We obtained institutional review board approval to perform a retrospective review of all patients who underwent ablation using IRE for hepatic tumors with margins within 1 cm of the common hepatic duct or the first-order branches of the common duct (the left and right hepatic duct before further branching) performed at our institution from January 2011 to September 2012. The shortest distance between the tumor margin and the closest bile duct was measured on CT images (LightSpeed 16/LightSpeed VCT; GE Medical Systems, Milwaukee, Wisconsin) obtained before ablation using axial, coronal, or sagittal reformations. Distance measurements were performed independently by two radiologists (T.W. with 7 y of experience, K.S.L. with 4 y of experience) (**Fig 1a–d**).

IRE Procedure

The tumors were targeted with IRE because of concern for duct stricture if a thermal technique was used. In all cases, the planning of the ablation zone was performed in a way that a minimum electric field of 680 V/cm would be achieved throughout the tumor, which would result in cell death by IRE (6).

IRE was performed using a commercially available direct current pulse generator device for clinical application (NanoKnife; AngioDynamics, Queensbury, New York). The device can deliver 3,000 V and 50 A through either 16-gauge or 18-gauge needle electrodes. Although any number of electrodes can be used to enclose a target fully with IRE, pulses are delivered through only two needles at any one time. Ablation zone size can be influenced by length of the active tip (0.5–4 cm), pulse number (typically 70–90), duration of pulses (typically 90–100 μs), distance between probes, and voltage applied.

All procedures were performed under general anesthesia with complete muscle blockade (paralysis) to reduce muscle stimulation from the treatment (although even with complete muscle blockade, local muscle stimulation in close proximity to the area treated by IRE is common). The patient's electrocardiogram was synchronized to the IRE device such that pulses were delivered during the complete refractory period (50 ms after the R wave) to prevent arrhythmias.

ELECTRODE PLACEMENT

Needle placement was performed under CT (LightSpeed 16) or positron emission tomography (PET)/CT (Discovery PET/CT 690; GE Medical Systems) guidance. Electrodes were placed such that the active exposed needle tip of each probe was approximately parallel to its companion. Image reconstructions along the electrode axis were performed to measure distance between the tips of the electrodes to adjust treatment parameters on the IRE planning console accordingly. The number of electrodes used depended on the size of the tumor and the operator. Needles were placed in a way to ensure complete coverage of the tumor, while avoiding direct puncture of critical structures such as blood vessels and bile ducts. The individual planning of electrode trajectories was at the discretion of the interventional radiologist performing the ablation. In this cohort of patients, the median number of probes used was three (range, two to six), with a median distance between probes of 1.6 cm (range, 0.8–3 cm), and an active exposure of 2.5 cm (range, 1.5–3 cm).

Device Setting

The median voltage applied per electrode pair was 2,370 V (range, 1,800–3,000 V) achieving an electrical field strength of 1,510 V/cm (range, 904–1,982 V/cm) between the electrodes. A minimum of 70 pulses (range, 70–90 pulses) applied in trains of 10 pulses with a minimum pulse length of 90 μs (range, 90–100 μs) was applied via each electrode pair. Repeat treatments were given until an increase of current was observed between the first pulse of each pulse set (indicating successful electroporation owing to pore formation represented as a reduction in electrical resistance). Technical treatment success was confirmed with split-dose PET/CT through resolution of fluorodeoxyglucose activity as previously described (14) or contrast-enhanced CT with a hypodense ablation zone encompassing the tumor.