CLINICAL STUDY

Percutaneous Ablation of Hepatic Tumors Using Irreversible Electroporation: A Prospective Safety and Midterm Efficacy Study in 34 Patients

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ABSTRACT

Purpose: To evaluate the safety and efficacy of percutaneous irreversible electroporation (IRE) of primary and secondary liver cancer unsuitable for resection or thermal ablation.

Materials and Methods: In this prospective, single-center study, 65 malignant liver tumors (hepatocellular carcinoma, n = 33; cholangiocellular carcinoma, n = 5; colorectal cancer metastasis, n = 22; neuroendocrine cancer metastasis, n = 3; testicular cancer metastasis, n = 2) in 34 patients (27 men, 7 women; mean age, 59.4 y ± 11.2) were treated. Local recurrence-free survival (LRFS) according to the Kaplan-Meier method was evaluated after a median follow-up of 13.9 months.

Results: Median tumor diameter was 2.4 cm ± 1.4 (range, 0.2–7.1 cm). Of 65 tumors, 12 (18.5%) required retreatment because of incomplete ablation (n = 3) or early local recurrence (n = 9). LRFS at 3, 6, and 12 months was 87.4%, 79.8%, and 74.8%. The median time to progressive disease according to modified Response Evaluation Criteria In Solid Tumors was 15.6 months. Overall complication rate was 27.5% with six major complications and eight minor complications. Major complications included diffuse intraperitonal bleeding (n = 1), partial thrombosis of the portal vein (n = 1), and liver abscesses (n = 4). Minor complications were liver hematomas (n = 6) and clinically inapparent pneumothoraces (n = 2).

Conclusions: IRE showed promising results regarding therapeutic efficacy for the percutaneous treatment of liver tumors; however, significant concerns remain regarding its safety.

ABBREVIATIONS

CTCAE = Common Terminology Criteria for Adverse Events, IRE = irreversible electroporation, LRFS = local recurrence-free survival, mRECIST = modified Response Evaluation Criteria In Solid Tumors

Because of its theoretical safety advantage over thermal ablative techniques, irreversible electroporation (IRE) has gained popularity for percutaneous tumor ablation, and it is currently used to treat tumors in locations where thermal ablation is contraindicated. However, its possible benefits should not be overestimated. Despite the assumption of the nonthermal nature of IRE, it has been shown that, if parameters are not chosen correctly, IRE may produce sufficient heat to induce coagulation necrosis under some conditions of high intensity (1–3). Moreover, the current IRE technology appears to be substantially affected by tissue properties and structure,

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which might also influence the size and shape of the ablation area and hinder complete tumor destruction. In addition, the size of the ablation zone depends on many technical parameters, such as electrode spacing, relative position of electrodes, length of the active tip, pulse number and duration, and applied voltage. For this reason, the precise placement of at least two (usually four to six) electrodes in parallel is technically more challenging compared with conventional ablation techniques and may raise further challenges for effective tumor ablation (4).

Nonetheless, preclinical studies using animal models have shown the efficacy of IRE for ablation of hepatic tissue (5) and hepatocellular carcinoma (6). However, clinical data regarding safety and efficacy of IRE in the treatment of liver tumors in humans are limited (7–9). Scheffer et al (10) were the first to prove the histopathologic efficacy of IRE in humans with colorectal liver metastases in an ablate and resect trial. They found IRE to cause avitality of tumor cells within the ablation zones 1 hour after treatment. The aim of the present study was to contribute to current knowledge by prospective evaluation of the safety and of midterm efficacy of percutaneous IRE in patients with primary and secondary liver cancer in a clinical setting.

MATERIALS AND METHODS

Approval of the institutional review board was obtained for this prospective single-center study. From December 2011 to June 2013, 65 target tumors in 34 patients with primary or secondary liver cancer were percutaneously treated in 51 procedures (Table 1). Seven women (20.6%) and 27 men (79.4%) were included. Mean age of the patients was 59.4 years ± 11.2 (range, 22–81 y). Patients were selected for IRE if surgical resection or thermal ablation was precluded, and each patient's case was discussed in a multidisciplinary tumor conference to ensure that all treating physicians from the disciplines of medical oncology, radiation oncology, gastroenterology, interventional radiology, nuclear medicine, and surgery agreed with the proposed treatment plan. Table 2 shows inclusion and exclusion criteria for this prospective study.

Table 1. Demographic Data

Variable	Value	Range
Total no. patients	34	
Median follow-up (mo)	13.9	1.8–19.5
Treated tumors	65	
Tumors treated per patient	1.91	1–4
Mean age (y)	59.4	22–81
Sex		
Men	27 (79.4%)	
Women	7 (20.6%)	
ECOG/Karnofsky performance status		
ECOG 1 (100%–70%)	23 (67.7%)	90%–40%
ECOG 2 (60%–50%)	8 (23.5%)	
ECOG 3 (40%–30%)	3 (8.8%)	

ECOG = Eastern Cooperative Oncology Group.

The most frequent diagnoses were hepatocellular carcinoma (n = 15 patients, n = 33 tumors) and colorectal liver metastases (n = 12 patients, n = 22 tumors). Other tumor types included cholangiocellular carcinoma (n = 4 patients, n = 5 tumors), metastasis of testicular cancer (n= 1 patient, n = 2 tumors), and metastatic neuroendocrine tumors (n = 2 patients, n = 3 tumors). Before IRE treatment, complete staging consisting of contrast-enhanced computed tomography (CT) scan of the chest, abdomen, and pelvis and dedicated magnetic resonance (MR) imaging of the liver with gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Primovist; Bayer Pharma AG, Berlin, Germany) was performed during the patients' admission examinations (Fig 1).

Tumor Characteristics

The median largest diameter of the target lesions before ablation was 2.4 cm ± 1.4 (minimum 0.2 cm, maximum 7.1 cm) with a mean volume of 10.2 cm^3 ± 17.0 (minimum 0.13 cm^3, maximum 124.1 cm^3). Of the 65 target lesions, 29 tumors were located in segments II, III, IVa, and IVb; 25 tumors were located in segments V and VI; and the remaining 11 tumors were located in segments VII and VIII (Table 3).

Demographic Data

Prior therapies of patients included surgical treatment (20 patients; 58.8%); systemic therapy (15 patients; 44.1%); and liver-directed therapies, such as radiofrequency ablation (seven patients; 20.6%), hepatic arterial therapy (four patients; 11.8%), and radiation therapy (three patients; 8.8%). Most patients with hepatocellular carcinoma had preserved liver function: seven patients with Child-Pugh class A (46.7%), six patients with Child-Pugh class B (40.0%), and two patients with Child-Pugh class C (13.3%).

Electroporation Protocol

The IRE procedures were performed with the NanoKnife device (AngioDynamics, Latham, New York) and were carried out in accordance with the manufacturer's guidelines. Patients received general anesthesia, mechanical ventilation, and neuromuscular blocking. Treatment planning was based on the measurements of CT imaging performed before the intervention. Depending on tumor size and shape, the desired zone of tissue ablation to ensure a 1-cm safety margin around the entire tumor was entered into the generator. The number of required IRE electrodes (range, two to six) and their relative position to each other were planned on the IRE device.