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Intraoperative adverse events during irreversible electroporation–a call for caution

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Abstract

BACKGROUND: Irreversible electroporation is increasingly used for treatment of solid tumors, but safety data remain scarce. This study aimed to describe intraoperative adverse events associated with irreversible electroporation in patients undergoing solid tumor ablation.

METHODS: We analyzed demographic and intraoperative data for patients (n = 43) undergoing irreversible electroporation for hepato-pancreato-biliary and retroperitoneal malignancies (2012 to 2015). Adverse events were defined as cardiac, surgical, or equipment-related.

RESULTS: Adverse events (n = 20, 47%) were primarily cardiac (90%, n = 18), including blood pressure elevation (77%, n = 14/18) and arrhythmia (16%, n = 7/43). All but one was managed medically, 1 patient with arrhythmia required termination of ablation. Bleeding and technical problems with the equipment occurred in 1 patient each. Multivariable analysis revealed previous cardiovascular disease and needle placement close to the celiac trunk associated with increased likelihood for cardiac events.

CONCLUSIONS: Intraoperative cardiac adverse events are common during irreversible electroporation but rarely impair completion of the procedure.

The introduction of new nonthermal ablation therapy, mostly targeting perivascular unresectable solid tumors typically not amenable to other ablation modality, has triggered significant interest from many surgeons and interventional radiologists. A few authors have explored this new tool with caution and have designed protocols to secure safe use and establish therapeutic boundaries.[1] Irreversible electroporation (IRE) technique is based on series of microsecond electrical pulses exposing malignant cells to high-field electrical pulse leading to cell membrane damage and consecutive death.[2,3]

The main advantage of IRE over other approaches is the avoidance of thermal injury to the surrounding structures, thereby sparing essential structures such as nerves, vessels, and bile ducts.[3–6] This has offered new horizons for the

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treatment of selective types of hepato-pancreato-biliary (HPB) tumors, mostly for local advanced pancreatic cancer, with emerging results suggesting improved overall survivals with the use of IRE.[6–11]

Despite these beneficial characteristics of IRE, potential risks of this new technique include the requirement of general anesthesia, the use of high voltage with particular caution in patients with preexisting cardiac arrhythmia and possible induction of epileptic seizures. The use of electrocardiogram (ECG) synchronization is mandatory to avoid fatal complications. Even taking all necessary safety steps, few studies reported peri-procedural adverse events.[1,12–14] These events range from mild hypertension to hemodynamically relevant arrhythmias, jeopardizing patient safety, and delivery of the energy required for a successful tumor ablation. The understanding of such intraoperative complications as well as a rapid and appropriate management is of paramount importance for patient safety, particularly in the older population suffering from unresectable tumor associated with various comorbidities.[13,14]

The aims of the study were to describe intraoperative adverse events (IAEs) associated with IRE in patients presenting with HPB and retroperitoneal solid tumors and to identify risk factors for such adverse events.

Methods

Patients

Patients undergoing open or percutaneous IRE for HPB and retroperitoneal malignancies between September 2012 and December 2015 in our institution were prospectively included in a database. The study was approved by the institutional review board of the University Hospital of Zurich. Exclusion criteria to proceed with IRE in our center included patients with epilepsy, the use of antiarrhythmic medication, or the presence of an implantable neurostimulator or pacemaker. Patient selection was finalized during our weekly multidisciplinary tumor board. Indications included perivascular unresectable liver tumors, unresectable perihilar cholangiocarcinoma and intrahepatic cholangiocarcinoma, locally advanced pancreatic cancer, and perivascular retroperitoneal tumors. In addition comorbidities were recorded in each patient. Cardiovascular disease was defined as the presence of cardiomyopathy, coronary artery disease, history of myocardial infarction, previous coronary revascularization, hypertensive heart disease, or cardiac dysrhythmias. Diabetes mellitus type 2 was defined as insulin-resistant, noninsulin dependent, and adult-onset diabetes requiring oral hypoglycemic agents or insulin injection. Chronic kidney disease was defined as glomerular filtration rate less than 60 mL/min/1.73 m^2 for 3 months or more. Because majority of patients with a medical history of diabetes mellitus (88%, n = 7/8) simultaneously suffered from cardiovascular disease, this group was categorized as cardiovascular disease associated with diabetes.

Anesthetic protocol

All procedures were performed under general anesthesia using propofol, fentanyl and rocuronium for induction and sevoflurane for maintenance according to an anesthetic standard operating procedure. Preoperative monitors were placed, including 5-lead ECG, invasive arterial blood pressure, pulse oximetry, bispectral index–monitoring electrodes, and multifunction defibrillation electrodes (Medi-Trace Cadence, Covidien, Mansfield, MA, USA) placed antero-laterally. A second 5-lead ECG was connected to the IRE machine through the Accusync device for cardiac synchronization. Neuromuscular blockade was monitored by train of 4 stimulations. Train of four (TOF) response greater than or equal to 1 was corrected with additional application of rocuronium (5 mg intravenous [i.v.]). Before initiating the IRE procedure, complete neuromuscular blockage was explicitly confirmed by the absence of TOF response. In addition, during percutaneous IRE, short interruptions of mechanical ventilation were granted to minimize diaphragm movement, if necessary. Intraoperative continuous monitoring of blood pressure, heart rate, cardiac rhythm, and saturation was routinely performed. Intraoperative electrolytes were determined by blood gas analysis.

Irreversible electroporation procedure

All procedures were done by NanoKnife IRE System (AngioDynamics, Queensbury, New York). For open procedures, after explorative laparotomy with meticulous inspection of the abdominal cavity and exclusion of additional metastases, tumor measurement was followed by needle placement under ultrasound (intraoperative ultrasound) guidance (BK Medical, Flex Focus, Siemens). Percutaneous procedure was performed by interventional radiologist dedicated to IRE procedure. Computer tomography fluoroscopy (Somatom Definition AS, 64 slices Siemens) guided needle placement was complemented by intraoperative ultrasound if necessary. Needle position and spacing were confirmed before starting ablation. By default, the delivered voltage was 1,500 V/cm, at a pulse interval of 70 microseconds per pulse, for initial planned 90 pulses. The pulses were synchronized with the heart rate.

Intraoperative adverse events

IAEs during IRE were defined as surgical, technical, or of cardiac origin. Surgical type included any iatrogenic injury due to needle placement. Intraoperative problems due to malfunctioning of the equipment were classified as technical complications. Cardiac adverse events included arrhythmia and arterial hypertension. After ensuring that the patient was adequately anesthetized, systolic blood pressure elevations of greater than 20% from baseline blood pressure was labeled as intraoperative hypertension. Arrhythmia was considered hemodynamic relevant if