รายงานผู้ป่วย • Case Report

Anesthetic Management, Complications, and Postprocedural Pain in Patients Undergoing Percutaneous Irreversible Electroporation (IRE) in Siriraj Hospital: A Case Series Report

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Background: Irreversible electroporation (IRE) is not a familiar procedure to Thai anesthesiologists and is a relatively new alternative for treatment in patients with soft tissue tumors. This technique is considered a treatment arising from a new area of medicine that incorporates the principle of pulsed high-voltage engineering and cell biology. To date, there are still no definite anesthetic management guidelines for IRE.

Objective: This study was designed to describe IRE anesthetic management and complications as well as postprocedural pain in Siriraj Hospital.

Methods: In order to investigate IRE perioperative management and complications, the retrospective data of 14 patients who were scheduled for initial treatment in setting up IRE procedure in the Faculty of Medicine, Siriraj Hospital, were collected during 6 month-period (October 1, 2015 to March 31, 2016).

Results: The patients' mean age was 65.5 years old (range 53-75 years old). Eight patients were diagnosed with primary hepatic tumors, while the others had tumors from metastatic lesions. All the cases were operated under general anesthesia with endotracheal intubation. The intraprocedural complications, including hypo/hypertension, bradycardia, and cardiac arrhythmia, are discussed in this report as well as the postoperative pain scores. No life-threatening complications were observed.

Conclusion: IRE procedure required general anesthesia with endotracheal intubation and vigilant observation for hemodynamic instability, arrhythmia and pain. Moreover, close communication between the anesthesiologists and radio interventionists are a prerequisite for optimal patient care and for the minimization of adverse events.

Keywords: anesthetic management, complications, hepatocellular carcinoma (HCC), irreversible electroporation (IRE), postprocedural pain

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Irreversible electroporation (IRE) is a relatively novel heat-independent ablation procedure for benign or malignant tumors in lieu of open surgery. By a process known as electroporation, IRE utilizes multiple cycles of short (micro to millisecond) pulses with high voltage electrical current to disrupt the integrity of tumor cells through destabilization of polarized lipid bilayers on the inner surface of the cell membrane, without damaging healthy extracellular tissue close by[1,2] IRE relies on a bioelectric basis that combines the principle of high voltage electrical engineering with cell biology.[3-6] The procedure delivers a pulsating direct electrical current of 20 to 50 Ampere (A) and 500 to 3,000 Volts (V) to primary or metastatic tumors of the liver, kidney, pancreas, or lungs. The released pulsed electrical field can alter the transmembrane potential of cells by increasing cell membrane permeability. The electrical field magnitude and number and duration of the pulses are important factors that alter the survival rate of the affected cells.[3,7] The IRE procedure is more effective

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than radio frequency ablation (RFA) in some conditions, in terms of causing no damage to peripheral tissue and associated vital structures, such as blood vessels and bile ducts, based on the heat generated, with no 'heat sink' effect as usually occurs in RFA when performed in proximity to major vasculatures, and its shorter treatment time and higher success rate for large lesions.[1,3,8-10] Moreover, IRE ensures nearly complete tumor ablation with a very low rate of recurrence.[7] Despite having some advantages over other techniques, besides RFA[2,7,11-13] (Appendix), the high voltage electrical stimulation during IRE ablation may lead to intraprocedural cardiac arrhythmias, severe muscle contractions, and seizures.[14] Therefore, specific and vigilant perioperative care is a prerequisite. According to previous studies, general anesthesia with the use of neuromuscular blocking agents (NMBAs) is required.[3,7,14,15] After standard monitoring, including non-invasive blood pressure (NIBP), a pulse oximeter and 5-lead ECG are placed, with the ECG leads connected to an ablation machine so that the IRE pulses could synchronize with the cardiac refractory period to prevent arrhythmias.

Initially, the mainstream treatments for solid organ tumors in the Faculty of Medicine, Siriraj Hospital were RFA, microwave ablation (MWA) and transarterial chemoembolization (TACE). Early percutaneous IRE procedures started to be performed in 2015. During that time, the practice of anesthesia was not well detailed for these novel techniques.

The present study investigated the intraprocedural anesthesia management, complications and treatment and also the postprocedural pain scores that were recorded during the initial 6 months after the percutaneous IRE establishment in our institution in order to develop practical institutional recommendations for further IRE interventions and to improve patient safety and perioperative care for IRE patients.

Methods

The retrospective case series study was conducted in the Faculty of Medicine, Siriraj Hospital. The patients scheduled for IRE were identified from electronic databases. Ethical Review Committee for Human Research, Institutional Review Board (IRB), Faculty of Medicine, Siriraj Hospital, Mahidol University (Si 270/2016) approval was obtained for a retrospective and observational patient review to be conducted and also the waiver of informed consents for this study. All the charts of 14 patients who were scheduled for IRE from October 1, 2015 to March 31, 2016 were reviewed. Exclusion criteria were: 1) patients with incomplete medical records and 2) patients with any changes that resulted in a cancellation of IRE treatment plans. Data concerning perioperative management, drug administration, and vital signs were recorded. Data on all complications, such as cardiac arrhythmias, perioperative hypo- or hypertensive episodes, self-report postoperative pain scores by numerical rating scale (NRS) 0-10, and treatments were collected. An arrhythmia is observed by abnormal electrocardiography (ECG) and is thus defined as accelerated, slowed or irregular heart rhythm. Intraoperative hypotension is defined as mean arterial pressure (MAP) <65 mmHg or a reduction of MAP or systolic blood pressure (SBP) ≥ 20% from baseline. Hypertension is defined as elevation of SBP ≥ 20% of preoperative value or the point where antihypertensive agent is administered to control the blood pressure.[16] Demographic data and clinical variables are summarized using descriptive statistics. Continuous variables are described as mean and standard deviation (SD). Relationship between 2 independent variables are determined by Pearson's correlation coefficient.

IRE procedures were conducted in a similar fashion to that previously described. [1,14] Briefly the procedure starts with computerized axial tomography (CT) scanning for identification of the tumor location. Needle electrodes, either bipolar or unipolar, are subsequently placed near the lesion under ultrasound or CT guidance. Short pulses with electrical current are delivered through the needles with the energy per pulses ranging from 0.2 Joules (70 µs, 5 A, 500 V) to 15 Joules (100 µs, 50 A, 3,000 V) in bursts of 80-90 pulses corresponding to the rhythm of the heartbeat. For a single large tumor or small multiple tumors, electrodes can be regularly

repositioned.[1,14] The patient's positioning before the procedure depends on the tumor location. In most cases with liver masses, the interventionists prefer to place the patients' arms above their head to improve the scanning quality.[3]

Results

During the 6-month study period, 14 patients were scheduled for IRE procedures in Siriraj Hoapital. No patients were excluded and therefore all were further analyzed. The epidemiological data demonstrated the study population could be categorized as American Society of Anesthesiologists (ASA) physical status classification 2-3. The mean age of the participants was 65.5±7.93 years old. The mean±SD of weight and height of the patients were 64.89±9.03 kilograms (kg) and 164.14±9.15 centimeters (cm), respectively, with an overall body mass index (BMI) of 24.10±2.92 kg/m^2. The tumors of the target organs for IRE primarily originated from the same organs or were the outgrowths as metastatic lesions. The locations and the volumes of the tumors as determined by imaging including ultrasound, magnetic resonance imaging (MRI), or computerized tomography (CT) scans varied among the individuals (Table 1). The study population comprised 11 males (78.57%) and 3 females (21.43%) and the majority, 8 persons (57.14%), were scheduled for IRE ablations of primary liver tumors. All the patients received standard monitoring care, comprising non-invasive blood pressure (NIBP) for at least every 5 minutes, continuous pulse oximetry, and electrocardiography (ECG). Of note, one patient, who was one of the very first IRE cases in Siriraj Hospital, acquired invasive blood pressure monitoring (arterial line) via the right radial artery to monitor the blood pressure fluctuations in a beat-to-beat fashion. Neuromuscular and brain monitoring, such as bispectral index (BIS), electroencephalogram (EEG), and train-of-four (TOF), were not applied to any of the patients. All the patients received general anesthesia with endotracheal tube (ETT). Intravenous propofol, fentanyl, and neuromuscular blocking agents (NMBAs) were administered during the induction phase. The depth of anesthesia was maintained with either sevoflurane or isoflurane, intravenous fentanyl, and NMBAs. Crystalloid solution, either 0.9% sodium chloride or acetate ringer solution, was administered intravenously during the operation. The fluid administration was summarized and divided by variables including the total body weight of the patients in kilograms and the total hours of the procedure to achieve the amount of fluid in milliliter/kilogram/hour (mL/kg/h). One patient (case 2) was administered with fentanyl and morphine during the maintenance phase. The total operative and total anesthesia times varied from 1.5 hours to 5.5 hours (mean 2.65 hours) and 2.75 hours to 6.25 hours (mean 3.49 hours), respectively (Table 2). Episodes of hemodynamic derangement, for example hypo- or hypertension as a consequence from the induction of anesthesia or intubation, were excluded in order to focus particularly on alteration of the hemodynamics during the IRE procedures. Ten patients (cases 2-5, 7-10, and 12-13, or 71.43% of all cases) developed hypotension with a systolic blood pressure (SBP) of 70-90 mmHg and diastolic blood pressure (DBP) of 40-60 mmHg. Along the course of IRE, however, only 6 individuals (cases 2-3, 7-9, and 12-13, or 60% of all hypotensive cases) required further treatment with intravenous ephedrine or norepinephrine. Meanwhile, 8 patients (cases 1-3, 7-8, 10, 12, and 14, or 57.14% of all cases) were observed with hypertension during the IRE procedures, with a systolic blood pressure (SBP) of 160-220 mmHg and diastolic blood pressure (DBP) of 75-110 mmHg, yet 4 persons (cases 1, 7, 10, and 14, or 50% of all hypertensive cases) required further treatment with titrated doses of intravenous nicardipine or esmolol. Sinus bradycardia during IRE was detected in 2 patients (cases 4-5, or 14.29% of all cases), who both required intravenous atropine to raise the heart rate. Premature ventricular contractions (PVCs) were detected in 2 patients (cases 1 and 8, or 14.29% of all cases), which in one of them (case 8) was accompanied by hypotension and therefore necessitated 6 mg of ephedrine, whereas bradycardia was found in the other patient (case 1) and, as a result, the patient needed 0.6 mg of atropine (Table 3). Fortunately,

no fatal arrhythmias, such as ventricular fibrillation (VF) and/or ventricular tachycardia (VT), were detected. No cases with severe muscle contraction that resulted in electrode dislocation or seizure were recognized. All the patients were discharged from the intervention suites uneventfully after the procedures.

Intraprocedural opioid consumption (Table 2) as well as the patients' pain scores at 2 and 6 h after the procedures were determined (Table 4). Fentanyl consumption during the maintenance of anesthesia after the start of the IRE procedure were summarized and divided by variables including the total body weight of the patients in kilograms and the total hours of the procedure to achieve a fentanyl dose in microgram/kilogram/hour (mcg/kg/h). One patient (case 2), who received 4 mg of morphine during anesthesia maintenance, was converted to an equivalent dose of 40 mcg of fentanyl.[15] The patients' postprocedural pain scores were not recorded upon observation in the recovery room after the procedure. However, there were no complaints about postprocedural pain or discomforts, therefore no medications for pain control were administered to any of the patients. Pain scores were then evaluated at 2 hours after IRE when the patients were transferred to the wards. Four patients (cases 1 and 10-12, or 28.57% of all cases) had moderate to severe pain intensity [Pain score 5-10 as reported by the patients using numerical rating scale (NRS)] and needed treatment at the wards. Various pain controls were administered, such as a nonsteroidal anti-inflammatory drug (NSAID), paracetamol, and opioids. The intensity of pain of all the patients who required treatment decreased to mild (Pain score 1-3) at 6 hours after the procedure.

Table 1 Preprocedural characteristics of the patients scheduled for IRE at Siriraj Hospital, Bangkok, Thailand (2015-2016).

Case	Sex	Age (Years)	Weight (Kg)	Height (cm)	BMI (Kg/m^2)	ASA	Underlying diseases	Primary tumor	Diagnosis	Location	Volume (cm^3)
1	Male	58	62.6	167	22.45	2	HT, CKD2	Liver	HCC	S8	5.04
2	Male	66	60	163	22.58	3	DM*, HT, DLP, CKD3	Liver	HCC	S5	0.51
3	Male	65	72	163	27.10	2	DM, HT, CKD2	Rectum	HCC	S8/5	60.2
4	Female	71	66	159	26.11	2	DM, HT	Liver	HCC	S5/6	8
5	Male	68	62	160	24.22	2	DM, HT, DLP, CKD3	Liver	HCC	S4a/8, S6	8, 3.43
6	Male	53	76	179	23.72	2	DM, CKD2	Liver	HCC	S7	3.71
7	Male	75	54.9	165	20.17	3	DM, HT, IHD, CKD3	Liver	HCC	S8	2.34
8	Male	54	73	169	25.56	2	HT, CKD3	Liver	HCC	S5/6/7/8	81.14
9	Female	70	63.9	146	29.98	2	HT, CKD2	Liver	HCC	S4b	1
10	Female	75	54	150	24.00	3	DLP, CVA, CKD2	Bile duct	CCA	S4b	10.03
11	Male	72	69	165	25.34	2	HT, CKD3	Sigmoid	HCC	S8/5	32.77
12	Male	56	64	172	21.63	2	CKD2	Pancreas	CA pancreas	Pancreatic neck	24.27
13	Male	60	82	178	25.88	2	CKD2	Colon	HCC	S4b	65.52
14	Male	74	49	162	18.67	3	DM*, HT, DLP, CKD2	Pancreas	CA pancreas	Pancreatic body	60
Mean±SD		65.50±7.93	64.89±9.03	164.14±9.15	24.10±2.92						

Abbreviation: ASA, American Society of Anesthesiologists physical status classification; BMI, Body mass index; CA, Cancer; CCA, Cholangiocarcinoma;

CKD2, Chronic kidney disease stage 2; CKD3, Chronic kidney disease stage 3; CVA, Cerebrovascular accident; DLP, Dyslipidemia; DM, Type 2 diabetes mellitus;

DM*, Type 2 diabetes mellitus with poor control; HT, Hypertension, Intrahepatic cholangiocarcinoma; HCC, Hepatocellular carcinoma; S, Hepatic segment;

IHD, Ischemic heart disease; SD, Standard deviation

Table 2 Intraprocedural anesthetic management for IRE at Siriraj Hospital Bangkok, Thailand (2015-2016).

Case	Anesthesia technique and ventilation	Anesthesia induction	Anesthesia maintenance	Intraoperative IV fluid (mL/kg/h)	Length of procedure (h)	Fentanyl consumption* (mcg/kg/h)
1	General, ETT, Controlled ventilation	Propofol/fentanyl/ cis-atracurium	Sevoflurane/fentanyl/ cis-atracurium	4.23 0.9% NaCl	2.5	0.8
2	General, ETT, Controlled ventilation	Propofol/fentanyl/ rocuronium	Sevoflurane/fentanyl/ morphine/rocuronium	1.31 Acetate Ringer solution	2.33	0.64
3	General, ETT, Controlled ventilation	Propofol/fentanyl/ atracurium	Sevoflurane/fentanyl/ atracurium	3.63 0.9% NaCl	2.75	0.38
4	General, ETT, Controlled ventilation	Propofol/fentanyl/ atracurium	Sevoflurane/fentanyl/ atracurium	2.53 0.9% NaCl	1.83	0.21
5	General, ETT, Controlled ventilation	Propofol/fentanyl/ atracurium	Sevoflurane/fentanyl/ atracurium	2.74 0.9% NaCl	2.66	0.15
6	General, ETT, Controlled ventilation	Propofol/fentanyl/ cis-atracurium	Sevoflurane/fentanyl/ cis-atracurium	2.63 Acetate Ringer solution	2.66	0.25
7	General, ETT, Controlled ventilation	Propofol/fentanyl/ cis-atracurium	Sevoflurane/fentanyl/ cis-atracurium	4.25 0.9% NaCl	1.5	0.31
8	General, ETT, Controlled ventilation	Propofol/fentanyl/ cis-atracurium	Sevoflurane/fentanyl/ cis-atracurium	1.19 Acetate Ringer solution	2.83	0.12
9	General, ETT, Controlled ventilation	Propofol/fentanyl/ atracurium	Isoflurane/fentanyl/ atracurium	4.90 0.9% NaCl	2.92	0.13
10	General, ETT, Controlled ventilation	Propofol/fentanyl/ atracurium	Sevoflurane/fentanyl/ atracurium	3.37 0.9% NaCl	2.17	0.43
11	General, ETT, Controlled ventilation	Propofol/fentanyl/ atracurium	Sevoflurane/fentanyl/ atracurium	3.07 Acetate Ringer solution	2.42	0.3
12	General, ETT, Controlled ventilation	Propofol/fentanyl/ atracurium	Sevoflurane/fentanyl/ atracurium	5.35 0.9% NaCl	2.17	0.54
13	General, ETT, Controlled ventilation	Propofol/fentanyl/ atracurium	Sevoflurane/fentanyl/ atracurium	4.13 0.9% NaCl	2.92	0.21
14	General, ETT, Controlled ventilation	Propofol/fentanyl/ atracurium	Sevoflurane/fentanyl/ atracurium	4.57 0.9% NaCl	5.5	0.19

Abbreviation: ETT, Endotracheal tube; h, Hour; IV, Intravenous; LV gr., Laryngoscopic view grading; 0.9% NaCl, 0.9% Sodium chloride solution; no., Number

*Fentanyl consumption during the maintenance phase of anesthesia.

Table 3 Intraprocedural adverse events and treatment for IRE at Siriraj Hospital Bangkok, Thailand (2015-2016).

Case	Baseline		Hypotension		Treatment		Hypertension		Treatment		Baseline	Abnormal ECG		Treatment
	SBP	DBP	SBP	DBP	E	NE	SBP	DBP	Nicar	Esmol	HR	Bradycardia	PVCs	Atropine
1	147	96	N/A	N/A	0	0	170	85	2.8	0	63	45	Yes	0.6
2	127	76	85	55	6	0	160	85	0	0	60	N/A	N/A	0
3	118	78	70	40	18	0	165	90	0	0	70	N/A	N/A	0
4	134	92	80	40	0	0	N/A	N/A	0	0	70	40	N/A	0.6
5	130	80	75	40	0	0	N/A	N/A	0	0	64	40	N/A	0.6
6	119	80	N/A	N/A	0	0	N/A	N/A	0	0	70	N/A	N/A	0
7	131	82	80	50	12	0	190	90	0.2	0	64	N/A	N/A	0
8	100	60	80	45	6	0	160	75	0	0	64	N/A	Yes	0
9	120	70	80	50	12	40	N/A	N/A	0	0	70	N/A	N/A	0
10	146	97	85	50	0	0	190	110	0.6	0	82	N/A	N/A	0
11	147	84	N/A	N/A	0	0	N/A	N/A	0	0	74	N/A	N/A	0
12	137	83	90	60	6	0	160	100	0	0	80	N/A	N/A	0
13	140	70	85	45	24	8	N/A	N/A	0	0	90	N/A	N/A	0
14	138	73	N/A	N/A	0	0	220	90	1.2	23	66	N/A	N/A	0

Abbreviation: DBP, Diastolic blood pressure (mmHg); E, Ephedrine (mg); Esmol, Esmolol (mg); HR, Heart rate; N/A, Not applicable (no events observed);

NE, Norepinephrine (mg); Nicar, Nicardipine (mg); PVCs, Premature ventricular contractions; SBP, Systolic blood pressure (mmHg)

Table 4 Postprocedural pain score assessed by the patient's numerical rating scale (NRS) and treatment for IRE at Siriraj Hospital Bangkok, Thailand (2015-2016).

Case	Pain score at 2 h	Treatment	Pain score at 6 h
1	8	Parecoxib 40 mg (oral)	3
2	2	none	0
3	3	none	0
4	2	none	0
5	2	none	0
6	0	none	0
7	0	none	0
8	2	none	0
9	0	none	0
10	8	Paracetamol 500 mg (oral)	2
11	10	Tramadol 25 mg (IV)	3
12	5	Pethidine 20 mg (IV)	1
13	0	none	0
14	3	none	0

Abbreviation: h, Hour; IV, Intravenous

Discussion

Even though it was discovered over a decade ago in 2007, IRE is still an innovative technique for non-invasive primary or metastatic tumor ablation in our institution and also in Thailand. At present, the indications of IRE are not well defined. Nevertheless, Månsson et al. reported some contraindications for this procedure as follows: 1) patients with a recent history of myocardial infarction, cardiac arrhythmias and epilepsy; 2) ablation of lesions of the eye and the eyelids; 3) lesions located near electronic or metal implantable devices; and 4) intrathoracic ablation for patients with a pacemaker or automated implantable cardioverter-defibrillator (AICD)[17] At Siriraj Hospital, patients were routinely screened by radio interventionists prior to the procedure.

Our study collected the perioperative data from the first 6 months of an initial phase of IRE set-up in the Faculty of Medicine, Siriraj Hospital. From the first IRE performance until July 2020, there were 52 scheduled cases in total, or around 11 cases per year. To date, there is no institutional anesthetic management guideline for IRE, so the practice is relatively similar to what was previously done in early cases, except for the invasive blood pressure monitoring by arterial-line. A comparison of anesthetic management between international institutions[1,3,14,18,19] and Siriraj Hospital is provided in Table 5.

Table 5 A comparison of the perioperative anesthetic management of percutaneous IRE between international institutions and the Faculty of Medicine, Siriraj Hospital, Mahidol University.

International institutions	Faculty of Medicine, Siriraj Hospital
Monitoring	
- Standard non-invasive monitoring + A-line	- Standard non-invasive monitoring ± A-line
- Capnography	- Capnography
- Train-of-four	
- Bispectral index	
- Temperature probe	
Anesthesia induction and maintenance agents	
- Fentanyl, Remifentanil, Sufentanil or Morphine	- Fentanyl ± Morphine
- Propofol	- Propofol
- Atracurium, Cis-atracurium, Rocuronium or Vecuronium	- Atracurium, Cis-atracurium or Rocuronium
- Sevoflurane, Isoflurane or Desflurane	- Sevoflurane or Isoflurane
Intraoperative management	
- Keep normovolemia	- Keep normovolemia
- Forced air warmer for upper & lower body	- ± Forced air warmer
- Determine zero twitch by Train-of-four	- Clinical observation for adequate muscle relaxation
- Beat to beat monitoring of blood pressure and arrhythmias by arterial-line	- Standard ECG monitoring
Postoperative pain control	
- Paracetamol, NSAIDs*, Opioid** or Patient Controlled-Analgesia (PCA)	- Paracetamol, NSAIDs***, Opioids****

*Diclofenac, **Piritramide or hydromorphone, ***Parecoxib, ****Tramadol or pethidine.

Despite being an ablation technology that guarantees less complications and more effective outcomes, the IRE procedure is not free from possible adverse periprocedural events when compared with other techniques (Appendix). Common complications can be listed as follows.

Cardiovascular effects

Hypertension

Patients usually experience transient hypertensive episodes during ablation cycles.[3,14,18] A study performed by Ball et al. suggested hypertension might persist for a few minutes but did not require any intervention[3], while other studies have mentioned opioids, fentanyl, or remifentanil as options for the management of hypertension.[14,18] In our study, our institution administered intravenous fentanyl during the induction phase of anesthesia and added additional doses in titration fashion provided that the patient's blood pressure was still over the normal range. Nicardipine injections were given in patients whose systolic blood pressure was higher than 180 mmHg or 20% higher than the baseline blood pressure. The patient with arterial-line monitoring (case 1) received a total dose as high as 2.8 mg of titrated nicardipine injection. Considering arterial-line as beat-to-beat blood pressure monitoring, the anesthesiologist could rapidly detect changes in the blood pressure values and was thus able to promptly prepare for aggressive hypertension treatment, leading to a high accumulated dose of nicardipine administration. One of the patients (case 14) also received a total of 1.2 mg of nicardipine and 23 mg of esmolol. This high antihypertensive dose might have been due to the long procedure, which lasted for 5 hours 30 minutes and the fact that esmolol is a short-acting agent.

Cardiac arrhythmias

Previous studies reported self-limiting cardiac arrhythmias during the IRE procedure, where ventricular extrasystole, bigeminy PVC, or a short run of ventricular tachycardia were noted [3,14], where the abnormal ECG rhythm returned to normal immediately at the end of each 10-pulse cycle. Our institution encountered 2 patients who experienced intraoperative non-fatal PVC episodes, which were accompanied with either hypotension or bradycardia (Table 3). To date, there is not sufficient evidence to determine the relationship between the electrical output and the occurrence of arrhythmias.[3]

Muscle contraction

A deep level of neuromuscular blockade is necessary for minimizing muscle contraction, which can lead to electrode displacement or trauma. Albeit there are no reported adverse events according to inadequate muscle relaxation, neuromuscular monitoring is recommended to ensure sufficient muscle relaxation.[3,18] Martin et al. suggested keeping a zero twitch of TOF before starting the IRE ablation process.[18] Nevertheless, TOF monitoring is not applied during the IRE procedure in our institution as we use clinical judgement of adequate muscle relaxation by observation of the resumption of spontaneous breathing according to the capnography patterns and the administration of NMBAs according to the time course of drug duration. Yet, none of the patients in our study had any complications as a result of inadequate muscle relaxation.

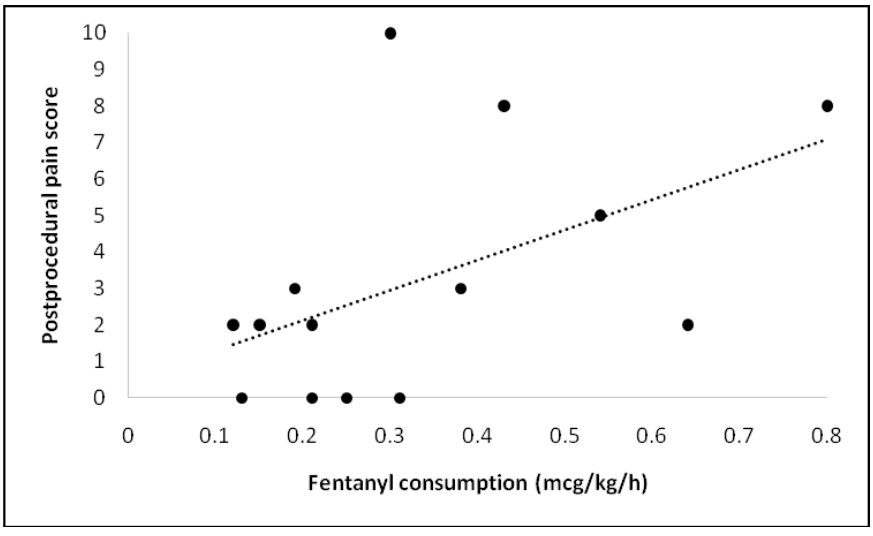
Seizures

There has been, so far, no cases of patients with epileptic activity during the IRE procedure.[14] Cerebral monitoring is not routinely performed; however, no patients with seizure episodes after IRE were reported in our institution.

Postprocedural pain

Several pain control measures for postprocedural percutaneous IRE have been proposed. Considering non-severe pain, intravenous opioid, NSAIDs or patient controlled-analgesia (PCA), and per oral paracetamol were reported to provide adequate pain control.[1,3,14,18,19] A previous study reported an overall mean pain score of 3 for percutaneous IRE of the liver, pancreas, kidney, and lesser pelvis. However, pain after pancreatic IRE was the most intense with a mean pain score of 4.[14] A study on the microwave ablation (MWA) of hepatic tumors proposed a correlation of a higher pain intensity

with several factors, such as ablation time > 20 minutes, increase in the amount of tissue volume, increase in Aspartate aminotransferase (AST) level > 250 U/L from baseline, number of lesions > 1, and location of the involved hepatic segments, especially segments 7/8.[20] Nevertheless, no correlations of post-IRE pain with the length of the ablation time, site of the lesion, and adequacy of muscle relaxation have yet been observed.[3] Surprisingly, our study found that the higher the fentanyl consumption during the IRE procedure, the greater the post-IRE pain intensity (cases 1, 10-12) (Figure 1; positive correlation determined by Pearson's coefficient (r) 0.51). We speculated that ablated lesions involving hepatic segment 8 and 4b might result in a higher degree of postprocedural pain, but not the volume of the lesion. One patient in our study with a tumor at the neck of the pancreas (case 12) also developed serious pain, which required pain control mediation. According to the limited number of cases in our study, it might not be sufficient to draw a definite conclusion on the relationship between the location of the tumor and postprocedural pain. However, it is worth further investigating whether this factor really has a connection to more severe pain, especially focused on a group of patients who have a lesion at hepatic segment 8 or 4b or pancreatic neck to see if they possibly need aggressive pain control and, perhaps, preemptive analgesia.



Pearson's correlation coefficient (r) 0.51

Figure 1 Correlation between intraoperative fentanyl consumption and postprocedural pain score

Conclusion

Current evidence on the safety of the IRE procedure is still inadequate. In addition, an anesthetic practice guideline for IRE has yet to be established. To the best of our knowledge, IRE requires general anesthesia with endotracheal intubation and controlled ventilation. The major concerns of this procedure include hypertension, cardiac arrhythmias, muscle contraction, seizures, and postprocedural pain. No major complications were detected based on the collected data from our study. A good comprehension about the procedural details and complications as well as close communication between anesthesiologists and radio interventionists are key considerations. Further research is required into appropriate periprocedural anesthesia management to achieve good outcomes and patient satisfaction.

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Appendix: A literature review of different techniques for percutaneous ablation of solid organ tumor

Comparison between techniques	Percutaneous ablation			
	IRE	RFA	MWA	Cryoablation
Mechanism	- Non-thermal ablation - Application of short pulses, high voltage electrical current through electrodes fixed in the target tissue, leading to pore formation in the cell membrane	- Production of frictional heating from alternating electrical current with high frequency to target tissue	- Rapid frictional movement of water molecules with high frequency in an electromagnetic field, causing heat in the target tissue	- Cold-induced intracellular crystal formation by argon followed by warm-induced crystal growth by helium passing through the same probes, resulting in cell death of the target lesion
Parameters	- Pulse length 100 microsec, 80-90 pulses/ treatment, 1,000-3,000 V/cm, 50 A	- Frequency 300-500 KHz	- Frequency 900-2,500 MHz	- 40°C for a few minutes
Advantages	- Limited thermal injury to surrounding tissues - No heat-sink effect - Good accuracy and predictable margin	- Predictable margin of ablated lesion - Long-known treatment	- Higher and faster to achieve target temperature - Great tissue penetration - Less chance of heat-sink effect - Can be used in variety of tissues	- Easy to monitor by visualizing the progression of ice balls
Limitations	- Novel technique with limited clinical data - Requires general anesthesia with NMBAs	- Heat injury to surrounding tissue - Thermal energy dispersal to blood flowing (Heat-sink effect) when ablation near major vessels	- No definite end point to set the energy for treatment	- Limited clinical data and proven efficacy - Cold-sink effect from nearby vessels - Variable ablation zone
Complications	- Spontaneous pneumothorax, pancreatitis	- Peritoneal hemorrhage, biliary or intestinal injury	- Peritoneal hemorrhage, biliary or intestinal injury	- Local hemorrhage, cold injury to surrounding organs - Cytokine-mediated cryoshock: fever, tachycardia, tachypnea

Abbreviation: A, Ampere; °C, Degree Celsius; KHz, Kilohertz; MHz, Megahertz; V/cm, Volts/centimeter