BMC Surgery

RESEARCH

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Real-world safety of irreversible electroporation therapy for tumors with nanoknife: MAUDE database analysis

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Abstract

Background Irreversible electroporation (IRE) is a non-thermal ablation technique using high-voltage, low-energy pulses to induce cell membrane perforation and cell death. As an emerging therapy, IRE has gained increasing application in local tumor treatment, with Nanoknife being the most widely used device. Despite its relative safety compared to traditional therapies, potential adverse reactions still merit the attention of clinicians.

Methods We analyzed all IRE-related adverse event reports in the Manufacturer and User Facility Device Experience (MAUDE) database, focusing on event types, Clavien-Dindo Grades, the timing of adverse events and temporal trends across cancers.

Results Device malfunctions with Nanoknife were a significant issue but have declined recently. In pancreatic cancer, gastrointestinal injuries (mainly hemorrhagic lesions) were most commonly reported. In liver cancer, arrhythmias were frequent, with no new cases in recent years. In prostate cancer, rectal fistula was the most common adverse event, with an increasing number of cases being reported.

Conclusions Theoretically, the Nanoknife is expected to exhibit favorable safety profiles. However, ongoing attention to device maintenance, treatment standardization, and postoperative management is needed to further enhance its safety.

Keywords Cancer, Irreversible electroporation, Nanoknife, IRE, Adverse events, Safety

Introduction

The high incidence and complex treatment of malignant tumors remain a significant challenge in the medical field. Traditional therapeutic modalities such as surgical resection, radiotherapy, and chemotherapy, despite their widespread application, are often associated with limitations including tissue damage, drug resistance, and systemic toxic side effects. While for tumors located adjacent to blood vessels and nerves, thermal ablation techniques may cause irreversible damage to surrounding tissues due to heat diffusion and can even lead to severe complications [1–3]. With the development of advanced medical technologies has revolutionized cancer treatment,

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with non-invasive focal therapies such as irreversible electroporation (IRE) emerging as promising options for precision cancer therapy. Unlike thermal ablation methods, IRE is a non-thermal energy platform which involves the use of high-voltage, low-energy electrical pulses to induce cell membrane permeabilization, leading to cell death, as well as spares surrounding functional structures such as blood vessels and nerves [4–10]. This unique technology has gained significant attention due to its potential to minimize invasiveness, reduce postoperative complications, and improve patient survival.

Although IRE is theoretically safer than conventional ablative therapy, its potential risks cannot be ignored [11]. For example, in treating malignant liver tumors, compared to thermal ablation techniques, although the incidence of complications is similar, there is still a certain risk of postoperative bleeding and other complications [12]. In pancreatic cancer, abdominal hemorrhage and vascular pseudoaneurysms were observed in the IRE group, and these complications were directly associated with IRE treatment and led to patient death [13]. Another study of patients with advanced pancreatic cancer showed a 25% rate of adverse effects in the IRE group, which included a variety of adverse outcomes such as infections, gastrointestinal bleeding, and ascites [14]. In additional, cardiac arrhythmias remained a critical concern, particularly in patients with preexisting cardiac conditions or implanted pacemakers [11]. Hence, the NCCN does not currently recommend IRE due to concerns regarding complications and technical expertise [15].

Table 1 An overview of the definition of the Clavien-Dindo grade classification

Clavien-Dindo Grade	Definition	Example
Clavien-Dindo 1	Any deviation from the normal postoperative course that does not require pharmacological treatment or surgical, endoscopic, or radiological intervention.	Mild postoperative discomfort, transient upper limb nerve dysfunction, and other similar conditions.
Clavien-Dindo 2	Requiring therapeutic interventions beyond Grade I medications, such as blood transfusion, total parenteral nutrition	Mild postoperative hypotension, anemia and other similar conditions.
Clavien-Dindo 3	Requiring surgical, endoscopic, or interventional treatments.	Gastrointestinal bleeding, intestinal obstruction, intra-abdominal infection, postoperative hemorrhage, and other related complications.
Clavien-Dindo 4	Life-threatening complications, including those involving the central nervous system and those requiring management in a surgical intensive care unit.	Acute myocardial infarction, multiple organ dysfunction syndrome (MODS), and other severe complications.
Clavien-Dindo 5	Patient death.	Postoperative mortality.

Currently, the devices used for IRE in clinical practice are mainly from United States and China. Chinese manufacturers have developed products such as the DophiN3000 and high-frequency irreversible electroporation (H-FIRE), demonstrating innovation in intelligent operation and minimally invasive procedures [11]. Besides, the Nanoknife system, developed by AngioDynamics, has been in clinical use for the longest duration. It received FDA approval in 2011 and has over a decade of global clinical validation, accumulating a substantial amount of clinical data and earning widespread international recognition [12, 13].

The Manufacturer and User Facility Device Experience (MAUDE) database, maintained by the FDA, serves as a valuable publicly accessible data source for monitoring the safety of medical devices. It includes data related to Nanoknife [16]. Previous studies, while also focusing on the safety of IRE treatment, have generally lacked detailed analyses of specific types of adverse reactions and in-depth discussions on the temporal trends of these events over the years [2, 7, 14]. In this study, we systematically retrieved all cases of adverse reactions in cancer patients treated with Nanoknife in MAUDE from 2014 to 2024. We characterized the adverse reactions by Clavien-Dindo grade (CDG) classification (Table 1), categorized the types of adverse reactions, and analyzed trends across different tumor types. Our findings elucidate the potential risk profiles associated with electroporation therapy, thereby offering novel insights and references for the design and application of electroporation devices and the clinical management of patients undergoing this treatment.

Methods

Data source

We searched the MAUDE database for several main electroporation device names currently in clinical use, including "Nanoknife, ""DophiN3000," and "H-FIRE," and found that only "Nanoknife" was currently searched in the MAUDE database. Upon detailed review of the case chronologies, we excluded 8 duplicate cases, 1 case involving a procedure performed in pigs, and 2 cases that did not involve IRE treatment, resulting in 98 patients. The temporal scope of these cases spans from 2014 to 2024. The process of patient information inclusion was illustrated in Fig. 1.

Data consolidation

Based on the event descriptions, we analyzed each adverse event individually. The events were evaluated according to the CDG, and the primary cancer type was identified through detailed surgical procedure

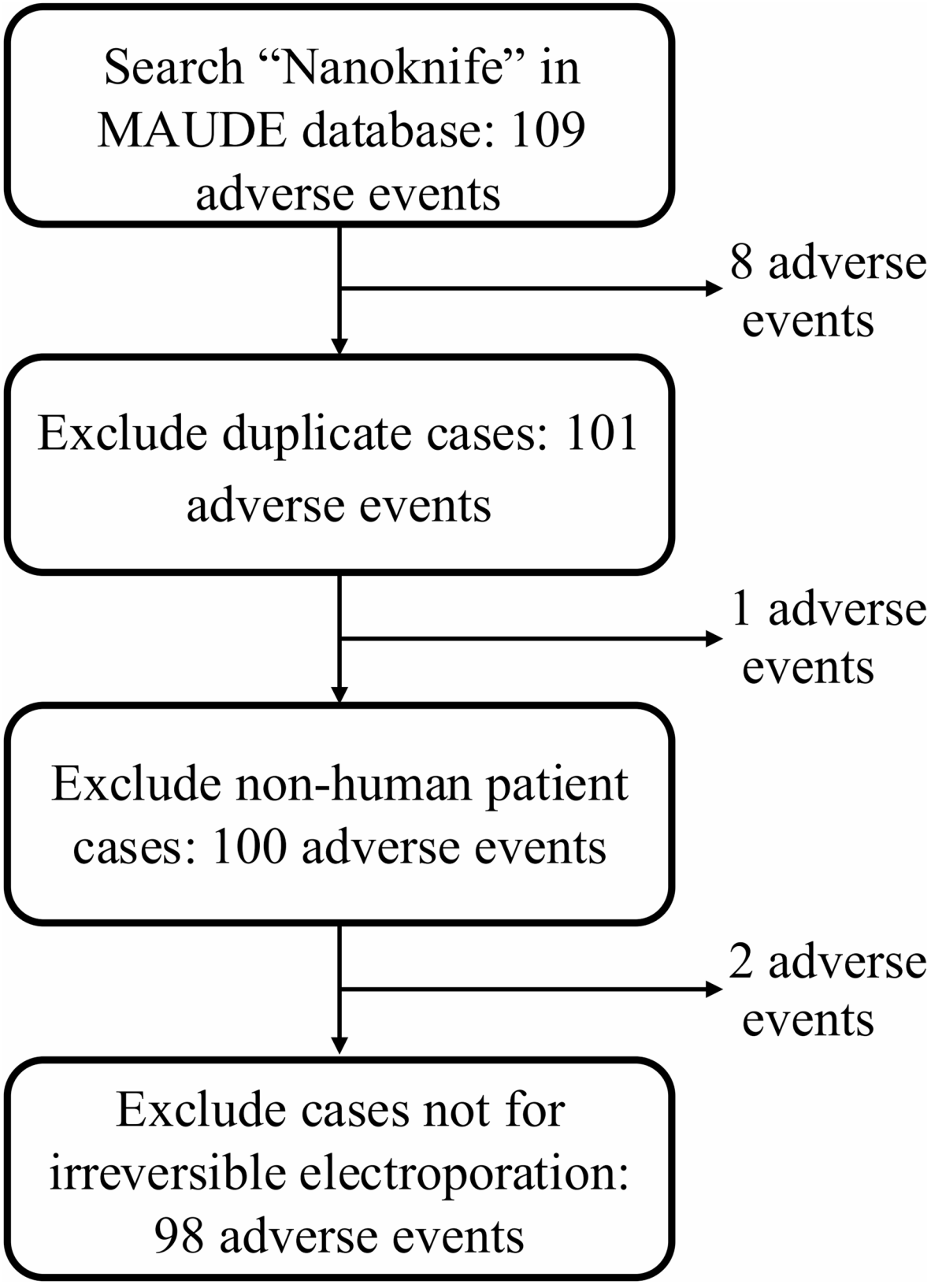

Fig. 1 The screening process of adverse effect cases

information. By statistically analyzing the frequency of each type of event, we summarized the types and trends of reported adverse events associated with Nanoknife treatment in MAUDE. Additionally, we have tabulated and analyzed the timing of adverse events following surgery.

Statistical analysis

The statistical analyses in this study primarily focused on the frequency and proportion of different types of adverse events. Data were analyzed and visualized using Excel and GraphPad Prism.

Results

Overview of included patients

Among the 98 patients included in our study from 2014 to 2024, there were 29 cases of pancreatic cancer, 19 cases of liver cancer, 10 cases of prostate cancer, 2 cases each of renal cell carcinoma, lung cancer, colorectal cancer, and esophageal cancer, 1 case of sarcoma, and 34 cases of other unspecified types of tumors. The distribution of CDG was as follows: CDG 1 in 42 cases (42.9%), CDG 2 in 19 cases (19.4%), CDG 3 in 25 cases (25.5%), CDG 4 in 6 cases (6.1%), and CDG 5 in 6 cases (6.1%) (Fig. 2A).

We also reviewed the temporal trends in the number of reported adverse events associated with electroporation therapy over the years. The incidence of adverse events peaked around 2020 and has since stabilized with a gradual decline in recent years (Fig. 2B). Notably, the frequency of CDG 3 events has shown a upward trend in recent years, while other CDG categories have remained stable or exhibited a downward trend (Fig. 2C). The specific types of adverse events in each tumor category are detailed in Table 2.

The most frequent adverse event was device malfunction, which prevented the equipment from initiating or operating properly. This issue prolonged the duration of surgery and anesthesia, thereby posing potential risks. However, it generally did not cause significant injury or symptoms in patients. These events were reported annually, peaking in 2018, and currently showed a declining trend with a relatively stable incidence (Fig. 3A). Regarding these events, Table S1 illustrated the specific causes of device failures occurring across different diseases.

Pancreatic cancer

Pancreatic cancer had the highest number of adverse events following IRE treatment, with a total of 29 cases (Fig. 1). The distribution of CDG among these cases was as follows: CDG 1 in 6 cases (20.7%), CDG 2 in 5 cases (17.2%), CDG 3 in 11 cases (38.0%), CDG 4 in 3 cases (10.3%), and CDG 5 in 4 cases (13.8%) (Table 2; Fig. 2D).

Among these cases, five were primarily due to device malfunctions that prevented normal initiation or usage. However, these issues had no significant impact on the patients postoperatively. Regarding bleeding events, there were six cases in total, two of which resulted in patient deaths. The bleeding sites were mainly concentrated in the ablation area (1 case), gastrointestinal tract (4 cases), and mesenteric artery (1 case). Notably, the onset of gastrointestinal and mesenteric bleeding was delayed, occurring during the postoperative recovery period (ranging from 1 to 4 weeks after surgery). Three patients developed thrombosis, with thrombi occurring in the mesenteric and other intra-abdominal vessels. One case of mesenteric thrombosis resulted in extensive ischemia and intestinal necrosis. Additionally, two patients experienced intestinal obstruction, and two had pancreatic duct injury. Other adverse events included arrhythmia, biliary obstruction, ascites, acute kidney injury, portal vein stenosis, severe pancreatic leak, skin discoloration/burn(s), bowel injury, gastro-duodenal artery aneurysm, heart failure/congestive heart failure, and bacterial infection, each occurring in one patient. In summary, among pancreatic cancer cases, gastrointestinal injuries and functional disorders were the most prevalent adverse events, comprising 11 cases (37.9%). The reported number of these events peaked in 2018, with no new cases reported in the past two years (Fig. 3B).

Liver cancer

Among the 19 adverse events following IRE treatment for liver cancer, the distribution of CDG was as follows: CDG 1 in 4 cases (21.1%), CDG 2 in 8 cases (42.1%), CDG 3 in 4 cases (21.1%), CDG 4 in 2 cases (10.5%), and CDG 5 in 1 case (5.3%) (Table 2; Fig. 2E).

The most commonly reported adverse events in liver IRE treatment were various types of arrhythmias, which accounted for 10 cases (52.6%). These included atrial fibrillation in 2 cases, ventricular fibrillation in 1 case, supraventricular tachycardia in 2 cases, ventricular tachycardia in 2 cases, bradycardia in 2 cases, and cardiac arrest in 1 case. Notably, all arrhythmia-related adverse events occurred between 2015 and 2019 (Fig. 3C). In addition to the arrhythmias, there were three cases of device malfunctions that led to prolonged surgical and anesthesia times. Two cases involved bleeding events. Other adverse events included portal vein stenosis, bacterial infection, and subcutaneous emphysema, each occurring in one case.

Prostate cancer

Among the 10 adverse events associated with IRE treatment for prostate cancer, the distribution of CDG was as follows: CDG 1 in 2 cases (20%), CDG 2 in 2 cases (20%), and CDG 3 in 6 cases (60%) (Table 2; Fig. 2F). The most frequent adverse event was rectal fistula, which occurred in six cases, all within the period from 2020 to 2024, with

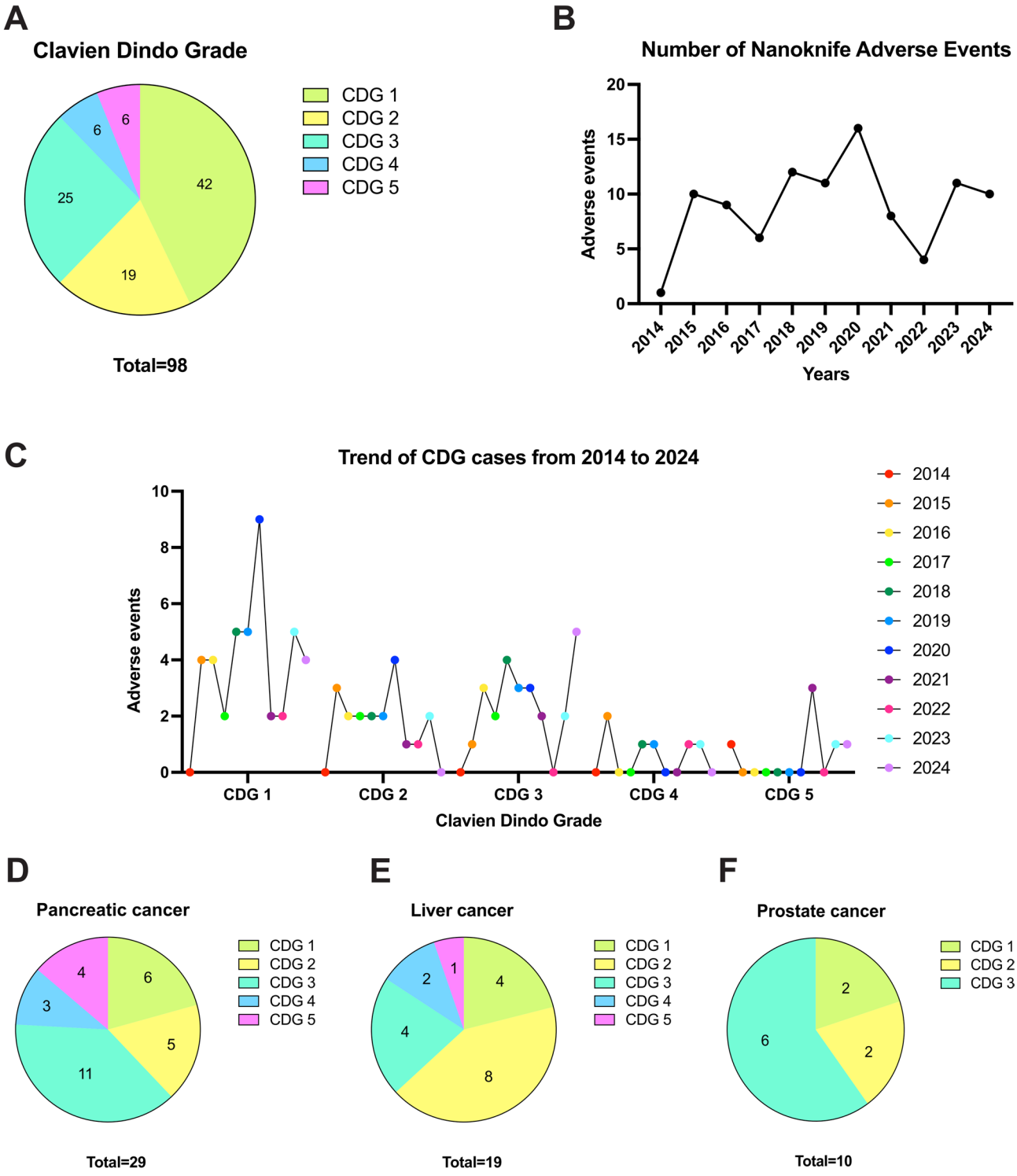

Fig. 2 Overview of the included cases. (**A**) The proportion of Clavien-Dindo Grade 1–5 in all cases; (**B**) The number of Nanoknife adverse events in each year; (**C**) The temporal trends of Clavien-Dindo Grade 1–5 events from 2014 to 2024; The proportion of CDG grading in (**D**) pancreatic cancer, (**E**) liver cancer, and (**F**) prostate cancer

an increasing trend in reported cases (Fig. 3D). Additionally, there were two cases of device malfunction that did not cause significant patient injury, one case of bradycardia, and one case of urinary tract infection.

Other cancers

In addition to the three aforementioned cancers, a few adverse events have been reported in other types of solid tumors. Renal cell carcinoma had two cases, including

Table 2 Nanoknife IRE for tumor indications, perioperative complications, and clavien Dindo grading from the MAUDE database

	Pancreatic cancer	Liver cancer	Prostate cancer	Renal Cell Carcinoma	Lung cancer	Colorectal Cancer	Esophageal cancer	Sarcoma	Tumor (unclassified)
Total	29	19	10	2	1	1	1	1	34
Clavien Dindo Grade									
1	6 (20.7%)	4 (21.1%)	2 (20.0%)	1 (50.0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	28 (82.4%)
2	5 (17.2%)	8 (42.1%)	2 (20.0%)	1 (50.0%)	0 (0%)	0 (0%)	1 (100%)	1 (100%)	1 (2.9%)
3	11 (38.0%)	4 (21.1%)	6 (60.0%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	3 (8.8%))
4	3 (10.3%)	2 (10.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.9%)
5	4 (13.8%)	1 (5.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.9%)
Adverse Events									
No Consequences Or Impact To Patient	5 (17.2%)	3 (15.8%)	2 (20.0%)	1 (50.0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	26 (76.5%)
Hemorrhage/ Bleeding	6 (20.7%)	2 (10.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)
Intestinal obstruction	2 (6.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Thrombosis	3 (10.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.9%)
Pancreatic duct injury	2 (6.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Arrhythmia	1 (3.4%)	10 (52.6%)	1 (10%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (14.7%)
Biliary obstruction	1 (3.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ascites	1 (3.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Acute kidney injury	1 (3.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Portal vein stenosis	1 (3.4%)	1 (5.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe pancreatic leak	1 (3.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Skin Discoloration/Burn(s)	1 (3.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)
Bowel injury	1 (3.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
Gastro-duodenal artery aneurysm	1 (3.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Heart Failure/Congestive Heart Failure	1 (3.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0%)	0 (0%)	0 (0%)	0 (0%)
Bacterial Infection	1 (3.4%)	1 (5.3%)	1 (10%)	0 (0%)	0 (0%)	2 (0%)	0 (0%)	0 (0%)	0 (0%)
Subcutaneous emphysema	0 (0%)	1 (5.3%)	0 (0%)	0 (0%)	0 (0%)	3 (0%)	0 (0%)	0 (0%)	0 (0%)
Paresis/Nerve damage	0 (0%)	1 (5.3%)	0 (0%)	0 (0%)	0 (0%)	4 (0%)	0 (0%)	0 (0%)	1 (2.9%)
Fistula	0 (0%)	0 (0%)	6 (60.0%)	0 (0%)	0 (0%)	5 (0%)	0 (0%)	0 (0%)	0 (0%)
Ureteral injury	0 (0%)	0 (0%)	0 (0%)	1 (50.0%)	0 (0%)	6 (0%)	0 (0%)	0 (0%)	0 (0%)
Failure of Implant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	7 (0%)	0 (0%)	0 (0%)	1 (2.9%)

one device malfunction (CDG 1) and one ureteral injury (CDG 2). Lung cancer had one case of device malfunction (CDG 1), colorectal cancer had one case of bowel injury (CDG 3), esophageal cancer had one case of bleeding (CDG 2), and sarcoma had one case of skin discoloration/burn(s) (CDG 2).

Unclassified cancers

In the MAUDE database, there were additional cases of IRE treatment for solid tumors where the specific tumor type was not clearly specified. We categorized these cases as "Tumor (unclassified)." A total of 34 such cases were identified, with the following distribution of CDG: 28 cases of CDG 1 (82.4%), 1 case of CDG 2 (2.9%), 3 cases of CDG 3 (8.8%), 1 case of CDG 4 (2.9%), and 1 case of CDG 5 (2.9%) (Table 2).

Among these cases, device malfunction was the most common adverse event, accounting for 26 cases (76.5%). Arrhythmias were observed in 5 cases (14.7%). Other adverse events included thrombosis, paresis/nerve damage, and failure of the implant, each occurring in 1 case (2.9%).

The timing of adverse events

We included a total of 43 adverse events with clearly defined timing. In Table 3, we have presented the timing of adverse events and categorized them based on when they occurred after Nanoknife treatment. Arrhythmia occurred predominantly during or immediately after surgery ($n = 16$), with additional cases observed at 20 min ($n = 1$) and 2 days ($n = 1$) post-procedure. Hemorrhage/bleeding ($n = 5$) and fistulas ($n = 3$) emerged as notable delayed complications, typically manifesting between 1 day and 2 months. Infectious complications (bacterial infections, $n = 2$) and vascular events (portal vein stenosis, $n = 2$; thrombosis, $n = 2$) were also documented, with onset ranging from 6 days to 2 months.

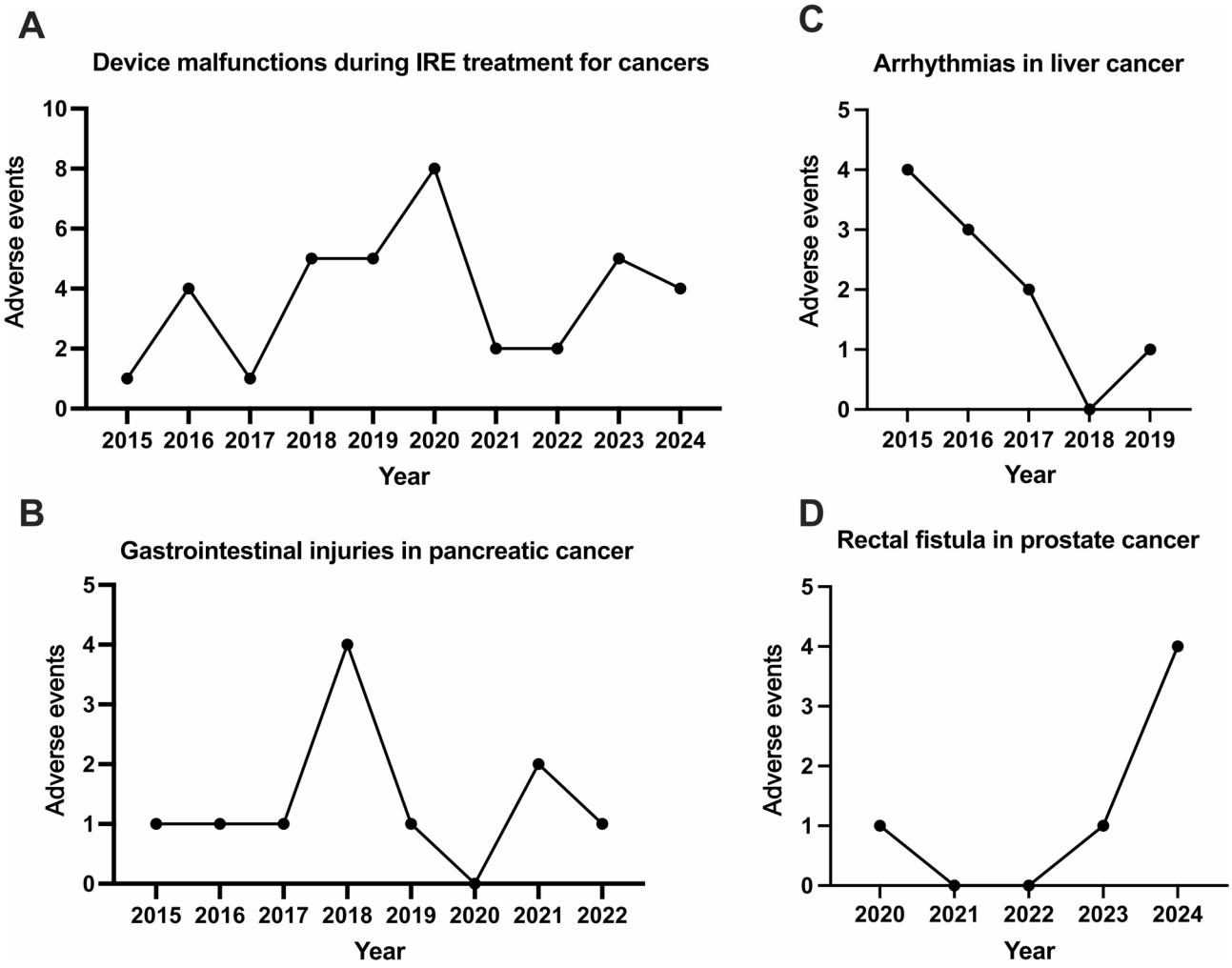

Fig. 3 The temporal trends of the major adverse events. (**A**) Temporal trends for device malfunction; (**B**) Temporal trends for gastrointestinal injures in pancreatic cancer; (**C**) Temporal trends for arrhythmias in liver cacner; (**D**) Temporal trends for rectal fistula in prostate cancer

Discussion

In this study, we utilized the MAUDE database for the first time to investigate the adverse reactions of IRE treatment across a wide range of solid tumors. Our findings revealed that device malfunction was the most common adverse event across various solid tumors. Among the major solid tumors treated with Nanoknife, pancreatic cancer was most frequently associated with gastrointestinal injuries, with bleeding being most frequently reported. In liver cancer, arrhythmias were the most reported adverse reactions. Meanwhile, rectal fistula was the predominant adverse event in prostate cancer. Additionally, we analyzed the temporal trends of adverse events over the years. Overall, despite the increasing application of Nanoknife in recent years, the number of reported adverse events has shown a stable decline. The timing data of adverse events underscored a bimodal pattern: acute intraprocedural adverse events (e.g., arrhythmia) and delayed complications (e.g., fistulas, infections), suggesting distinct mechanistic etiologies. These findings highlight the need for vigilant perioperative monitoring and long-term surveillance to mitigate risks associated with Nanoknife therapy.

Firstly, we found that device malfunction was the most common adverse event across various solid tumor treatments. Although it does not cause severe patient injury, it still poses potential risks. We found that the reporting of such events has gradually decreased in recent years and has shown a stable trend.

Nanoknife treatment is currently most widely applied in pancreatic, liver, and prostate cancers among the various cancer types treated with this technology. The most common adverse events in these three types of cancer are closely related to the anatomical locations of adjacent organs. In pancreatic cancer, gastrointestinal injuries are the most frequent. Although IRE theoretically offers better vascular protection, bleeding remains the most common adverse event in the treatment of pancreatic cancer

Table 3 The timing of adverse events following nanoknife treatment

The Timing of Postoperative Adverse Events	Disease	Adverse Events	Frequency
During the surgical procedure and Immediately Following the Surgery	Pancreatic cancer	Arrhythmia	1
		Portal vein stenosis	1
		Skin Discoloration/Burn(s)	1
		Thrombosis	1
	Liver cancer	Arrhythmia	10
		Subcutaneous emphysema	1
	Colorectal Cancer	Bowel injury	1
	Tumor (unclassified)	Arrhythmia	5
20 min	Prostate cancer	Arrhythmia	1
12 h	Pancreatic cancer	Hemorrhage/Bleeding	1
1 days	Pancreatic Cancer	Heart Failure/Congestive Heart Failure	1
	Liver cancer	Paresis/Nerve damage	1
	Sarcoma	Skin Discoloration/Burn(s)	1
	Tumor (unclassified)	Arrhythmia	1
2 days	Liver cancer	Hemorrhage/Bleeding	2
3 days	Liver cancer	Portal vein stenosis	1
6 days	Pancreatic cancer	Intestinal obstruction	1
7 days	Pancreatic cancer	Bacterial Infection	1
	Pancreatic Cancer	Intestinal obstruction	1
	Prostate cancer	Fistula	1
8 days	Pancreatic cancer	Gastro-duodenal artery aneurysm	1
9 days	Liver cancer	Bacterial Infection	1
12 days	Esophageal cancer	Hemorrhage/Bleeding	1
3 weeks	Prostate cancer	Fistula	1
1 month	Pancreatic Cancer	Hemorrhage/Bleeding	2
	Prostate cancer	Fistula	1
	Renal Cell Carcinoma	Ureteral injury	1
2 months	Tumor (unclassified)	Thrombosis	1

with Nanoknife. These findings are consistent with previous studies [7, 13], and Table S2 presented the current adverse event occurrence in the DIRECT cohort as mentioned on the AngioDynamics official website [13]. It is crucial to ensure that electrodes are accurately placed within the tumor to avoid contact with the gastrointestinal tract and other intra-abdominal organs. Postoperatively, enhanced management of bleeding risks and monitoring of gastrointestinal function are necessary.

In the liver cancer, the most common adverse reactions are various types of arrhythmias. This is primarily due to the anatomical proximity of the liver to the heart, where the electrical signals generated during IRE treatment can interfere with the normal electrical activity of the heart. This adverse reaction has been reported in previous studies [17]. Currently, the use of cardiac gating to synchronize IRE with the cardiac cycle has proven effective in avoiding such adverse events [18]. However, regrettably, we were unable to find any descriptions related to ECG gating in the MAUDE database. Therefore, we are currently unable to infer the risk of arrhythmias associated with Nanoknife treatment under ECG gating through the MAUDE database.

In prostate cancer, we identified that the most reported adverse event associated with Nanoknife treatment was rectal fistula. Previous studies have also reported rectal fistula as an adverse event following IRE treatment [19, 20]. Given that the prostate is anatomically distant from major abdominal vessels and vital organs, severe adverse events are relatively rare. Table S3 presented the current adverse event occurrence in the PRESERVE cohort as mentioned on the AngioDynamics official website. In the PRESERVE cohort, rectal fistula was also mentioned; however, the most common adverse event was hematuria. Although the study only established a definitive link between a small proportion of hematuria cases and Nanoknife treatment. Prior research has predominantly focused on comparing the urinary control and sexual function outcomes of IRE-treated prostate cancer patients with those undergoing traditional radical prostatectomy or other focal therapies [21]. It may be necessary to optimize surgical procedural standards and enhance postoperative management to mitigate this issue.

Since the MAUDE database currently lacks data on IRE devices other than Nanoknife, our analysis was restricted to Nanoknife-related cases. It is worth noting that compared to traditional IRE treatment with Nanoknife, the

next-generation technology, H-FIRE, may offer several advantages. Nanoknife is associated with limitations such as muscle contraction and incomplete ablation due to field drop-off. In contrast, H-FIRE can mitigate impedance-related field drop-off, thereby achieving more effective ablation [22]. Emerging studies have suggested that H-FIRE has a favorable safety profile [23–25]. However, no direct comparative trials have yet been conducted between H-FIRE and IRE treatments. Whether H-FIRE can alleviate the adverse events associated with Nanoknife, as identified in our study, is an important question that warrants further investigation.

However, the present analysis is constrained by the inherent limitations of the MAUDE database. Specifically, MAUDE encompasses voluntary reports dating back to June 1993, user organization reports beginning in 1991, distributor reports starting in 1993, and manufacturer reports from August 1996. In accordance with Part 803 of Title 21 of the Code of Federal Regulations of the United States, incidents that result in death, serious injury, or malfunction are mandated for reporting to the FDA. Conversely, the reporting of other incident types is voluntary. Furthermore, the database is susceptible to potential underreporting and misreporting biases, and the exact total number of IRE cannot be ascertained. As a result, the incidence of adverse events cannot be accurately inferred from the MAUDE database alone. Our study is limited to reflecting the temporal trends in adverse event reporting within MAUDE, thereby highlighting which adverse events may warrant focused attention. Nevertheless, the precise trends and current incidence rates of these adverse events necessitate further investigation through alternative study designs. Besides, another limitation of this study is the relatively small sample size. IRE is a relatively novel local ablation technique and is considered safer than other local therapies. Although its application has expanded annually, the number of reported adverse events remains limited. However, compared to previous IRE studies, which involved far fewer adverse event cases, our study provides a more comprehensive overview by consolidating data from 2014 to 2024. This approach allows for a better understanding of the types and trends of adverse events associated with IRE treatment.

Conclusion

By incorporating all adverse event reports related to Nanoknife treatment from 2014 to 2024 in the MAUDE database, this study systematically analyzed the frequency and temporal trends of adverse reactions across different cancers reported in MAUDE. We found that the overall reports of adverse events associated with Nanoknife treatment has been declining. However, gastrointestinal injuries in pancreatic cancer and rectal fistulas in prostate cancer remain areas of concern, as these adverse events continue to being reported with an increasing number in recent years. Our study provides new insights into the clinical application of IRE, suggesting that further improvements in device design, optimization of treatment protocols, and enhanced postoperative management could lead to enhanced safety profiles for IRE.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12893-025-03136-9.

Supplementary Material 1.

Acknowledgements
Not applicable.

Authors' contributions
Study Concept and Design: Jia-Cheng Xiang (JCX), Zhi-Yu Xia (ZYX), Shao-Gang Wang (SGW), Qi-Dong Xia (QDX) contributed to the conception and design of the study.Data Acquisition: Jia-Cheng Xiang (JCX), Jian-Xuan Sun (JXS) contributed to the acquisition of data.Data Analysis and Interpretation: Jia-Cheng Xiang (JCX), Zhi-Yu Xia (ZYX) performed the statistical analysis.Data Collation: Jia-Cheng Xiang (JCX), Zhi-Yu Xia (ZYX), collated the raw results. Data Visualization: Jia-Cheng Xiang (JCX), Qi-Dong Xia (QDX) visualized the data.Draft Writing: Jia-Cheng Xiang (JCX), Zhi-Yu Xia (ZYX) wrote the first draft of the manuscript.Manuscript Revision: Shao-Gang Wang (SGW), Qi-Dong Xia (QDX), Jia-Cheng Xiang (JCX) revised the manuscript. Equal Contribution: Jia-Cheng Xiang, Zhi-Yu Xia, Shao-Gang Wang, and Qi-Dong Xia contributed equally to this work.

Funding
Not applicable.

Data availability
The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 29 April 2025 / Accepted: 30 July 2025
Published online: 25 August 2025

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