Implantable cardioverter defibrillator treatment : benefits and pitfalls in the currently indicated population

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Chapter 15

Implementation of Lead Safety Recommendations

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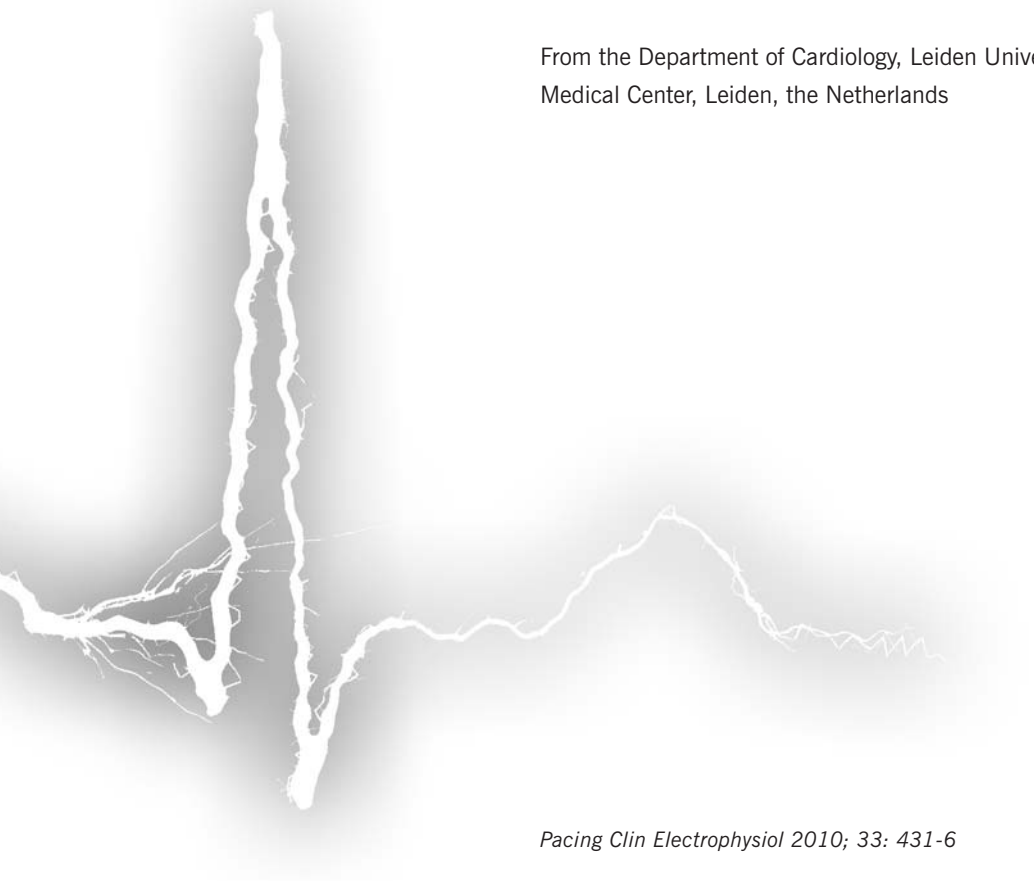

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Abstract

Background: The Medtronic Sprint Fidelis (SF) implantable cardioverter-defibrillator (ICD) lead has a higher than expected failure rate. Because of patient safety, Medtronic announced two advisories consisting of (1) adjustments in device settings (October 2007) and (2) installation of a lead integrity algorithm (May 2008). The objective of this study was to evaluate the effect of Medtronic's announcements on patient safety.

Methods: To comply with the advisories, two clinical evaluations were conducted. The effect of the advisories was assessed by the lead failure rate and the occurrence of inappropriate shocks due to lead failure. Three periods were distinguished in the comparison of event rates: lead implantation to advisory 1 (period A), in-between both advisories (period B) and advisory 2 to follow-up (period C).

Results: Since 2004, 372 patients received a Medtronic ICD and SF lead and were followed from first implant (December 2004) to April 2009. Cumulative incidence rate of lead failure was 3.6% [95%CI 1.6 – 5.6] at 21 months and increased to 11.0% [95%CI 6.1 – 15.9] at 42 months. After implementation of both advisories, the occurrence of inappropriate shocks due to lead failure decreased from 1.5 [95% CI 0.59, 3.00] per 100 lead-years in period A to 0.8 [95% CI 0.02, 4.25] per 100 lead-years in period C.

Conclusion: The current study demonstrates that despite an increasing risk for SF lead failure, implementation of the advisories decreased the occurrence of inappropriate shocks due to lead failure.

Background

Despite important life-saving advantages of implantable cardioverter-defibrillator (ICD) therapy, potential system-related complications pose major drawbacks.[1, 2] One of the most important being failure of the defibrillation lead, which can reach up to 20% in 10 year old leads.[3, 4] The 6.6 Fr Sprint Fidelis (SF) ICD lead (Medtronic Inc, Minneapolis, MN, United States) is an explicit example of a defibrillation lead with a higher than expected failure rate. Medtronic reported a failure rate of 2.4% 30 months after implantation and recent data demonstrate that the failure rate accelerates over time.[5, 6] In case of lead failure, up to 50% of the patients may experience inappropriate defibrillator shocks, which are painful and can potentially trigger ventricular arrhythmia and consequent death.[5, 7, 8]

In October 2007 – after 268.000 SF implants worldwide – Medtronic halted the distribution of the SF lead and issued recommendations on how to manage patients with SF leads and optimize patient safety.[9] Initially, the advisories included adaptation of device settings and activation of the Patient Alerts™. Later, in May 2008, Medtronic announced new uploadable software to increase the likelihood of fracture detection prior to inappropriate device discharges and suggested the use of remote monitoring (CareLink®).[10] In order to comply with these recommendations, all patients with a Medtronic ICD and SF lead were invited to the out-patient clinic for clinical evaluation and implementation of the advisories. Although the global compliance to advisories and safety alerts is increasing, relatively little is known about the effects of these recommendations in daily practice.[8, 11] We conducted two clinical evaluations in response to the advisories of the company and evaluated the results.

Methods

Advisory Implementation

Since 1996, all patients who received an ICD system at the Leiden University Medical Center, the Netherlands, were registered in the departmental Cardiology Information System (EPD-Vision®, Leiden University Medical Center). By using this database, all patients implanted with a Medtronic ICD and a SF Lead (Models 6949, 6948, 6931, 6930) were invited for implementation of the safety advisories. In accordance with the safety recommendations of Medtronic, two clinical evaluations were conducted. At each visit, patients were seen in a time period of one week. Both advisory implementations were based on the advisories of the company.

First Advisory

In agreement with the first advisory of Medtronic, the settings of the devices were adjusted.[9] The ventricular fibrillation detection for initial Number to Intervals to Detect (NID) was programmed to nominal settings (18/24) or longer at physician discretion and redetect NID to nominal settings (12/16). The Patient Alert™ for RV pacing, RV Defibrillation, and SVC Defibrillation impedance was turned on. Furthermore, the lead impedance alert threshold for RV Pacing was programmed to 1,000 Ω, if the typical chronic impedance for the patient is ≤ 700 Ω or to 1,500 Ω if the typical chronic impedance was > 700 Ω. For the RV Defibrillation and SVC Defibrillation the lead impedance alert threshold was set to 100 Ω.

Second Advisory

In May 2008, the Medtronic Sprint Fidelis Lead Performance Update announced uploadable software (i.e. lead integrity algorithm or LIA) to increase the likelihood of fracture detection prior to inappropriate device discharge and suggested the use of a remote monitoring system to facilitate remote access to the device information.[10] In case of a suspected lead failure, LIA automatically adjusts the programmed number of intervals to detect ventricular fibrillation to 30 out of 40 sensed beats and immediately initiates an audible alert. This warning signal will repeat every 4 hours and, if enabled, a wireless CareLink® alert is transmitted. Since LIA became available in September 2008, the second clinical evaluation was conducted in October 2008. During this visit, LIA was uploaded into all software compatible devices and the alert was tested for patient's audibility. Hereafter, remote monitoring was offered to all patients and, after acceptance, patients received a CareLink® Monitor. For evaluation of correct installation, all patients were asked to perform a test transmission at home. In case of technical installation problems, patients were offered on-site assistance.

Follow-up

Patients were followed from lead implantation, occurring between December 2004 and October 2007, to April 2009. Periodic device interrogation was performed every three to six months (after implementation of the first advisory every 3 months in all patients) and during these examinations, all leads were systematically screened for integrity. A lead was considered failed if one of the following criteria was met: (1) undersensing or oversensing of normal electrical cardiac activity; (2) incapability of sensing, pacing or defibrillation; or (3) inappropriate shocks secondary to electrical noise artifacts; (4) out-of-range lead impedance or LIA triggering an ICD alert.[5, 6] If a lead was removed or capped, the cause (lead failure or non-lead failure) was determined by the technician and medical supervisor. Furthermore, in case of lead failure, patient presentation and potentially triggered device alerts were assessed. Specifically, the occurrence of inappropriate shocks as the first sign of lead failure was noted. Finally, the feasibility of the safety advisories was evaluated.

Statistical analysis

Three periods were distinguished in the comparison of event rates: lead implantation to advisory 1 (period A), in-between both advisory (period B) and advisory 2 to follow-up (period C). Continuous data are expressed as mean and standard deviation or range; nominal data are presented as numbers and percentages. In the estimation of the 95% CI for event rates, a Poisson distribution of the observed number of events was presumed. To calculate standardized event-rates, the number of events during a period was divided by the follow-up in lead-years during that period. The cumulative incidence of SF lead failure was calculated using the Kaplan-Meier methodology.

Results

Patient characteristics

Between December 2004 and October 2007, 390 patients were implanted with a SF lead at the Leiden University Medical Center. In 18 (5%) patients a device by another manufacturer was implanted: 15 Biotronik (Berlin, Germany), 2 Guidant (St. Paul, MN, United States), 1 St Jude Medical (St Paul, MN, United States). The remaining 372 patients had a device manufactured by Medtronic and could therefore benefit for the advisories of Medtronic. The majority of the study population (n=372) was male (81%), and had ischemic heart disease (66%). Implanted SF leads consisted mostly of model 6931 (61%). Baseline patient characteristics are described in table 1. Patients were followed from implantation to April 2009 with an average follow-up period of 2.5 ± 1.0 years. During this period, 45 patients died. To our knowledge, no patients died as a direct or indirect result of lead failure. In all 45 patients, the leads were intact at their last follow-up.

Table 1. Baseline clinical characteristics at implantation of 372 patients with a Sprint Fidelis lead and a Medtronic ICD

Age (yr)	62 ±12 (range 17 – 85)
Male gender (n)	301 (81%)
ICD indication	
Primary prevention (n)	272 (73%)
Secondary prevention (n)	100 (27%)
LVEF (%)	31 ± 14 (range 4 – 80)
Ischemic heart disease (n)	246 (66%)
SF lead model (n)	
6930	1 (1%)
6931	229 (61%)
6948	45 (12%)
6949	97 (26%)

Continuous variables are expressed as mean ± SD. ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction.

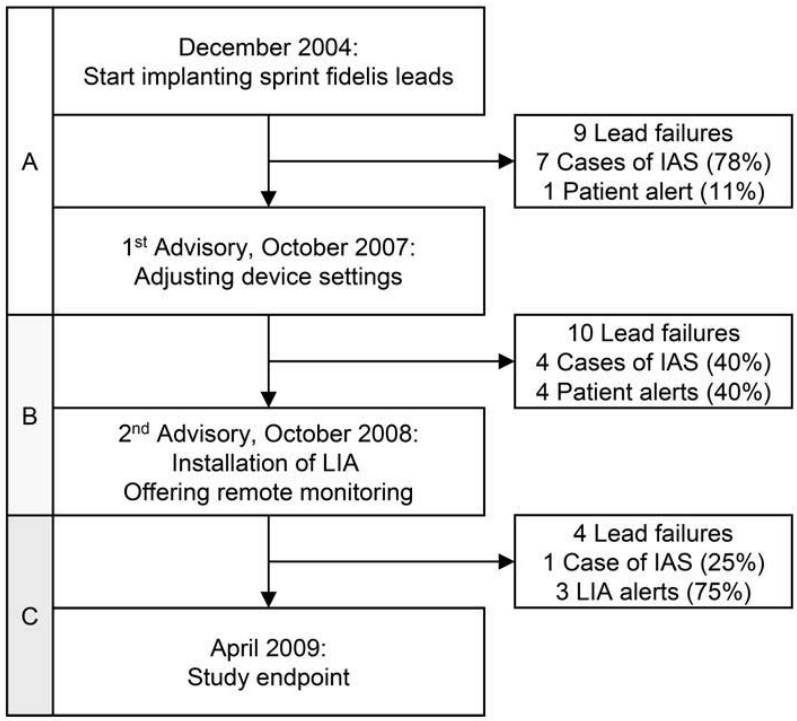

Figure 1. Flow chart showing the occurrence of lead failures, inappropriate shocks due to lead failure (IAS) and the triggered lead failure alerts which warned the patients before the occurrence of inappropriate therapy.

Period A

Prior to the first advisory, 372 patients were implanted with a SF lead and Medtronic ICD. Twenty-eight (8%) patients died and 15 (4%) leads were removed or capped of which 9 (2%) due to lead failure. In case of lead failure, 7 patients presented with inappropriate shocks, 1 patient was warned by the Patient Alert™ before an adverse event could occur and 1 patient was identified during routine device interrogation. (Figure 1 and table 2). Out of 15 removed leads, 5 were replaced by a new SF lead.

Consequently, 334 patients (including the 5 patients with a new SF lead) received an invitation for the first clinical evaluation. Since 4 patients were under supervision of another hospital, 330 patients attended. The recommended device programming changes were implemented in all attendees.

Period B

In-between both advisories, another 16 (5%) patients died and 15 (5%) leads were removed. Ten (3%) cases were classified as lead failure of which 4 cases presented with inappropriate shocks (range 1-25 shocks per patient), 2 cases were discovered by routine

Table 2. Lead failure characteristics for 23 Sprint Fidelis lead failures

No.	First findings	Cases of IAS	Number of IAS	Alert	Alert type	Implemented advisory
1	P/S impedance 2768 Ω	No	-	Yes	Patient Alert	-
2	Low P/S impedance	No	-	No	-	-
3	P/S impedance 1500 Ω	Yes	12	No	-	-
4	Noise P/S	Yes	1	No	-	-
5	Noise P/S	Yes	8	No	-	-
6	Noise P/S	Yes	18	No	-	-
7	Noise P/S	Yes	1	No	-	-
8	Noise P/S	Yes	2	No	-	-
9	Noise P/S	Yes	6	Yes	Patient Alert	-
10	P/S impedance 1504 Ω	No	-	Yes	Patient Alert	1
11	Noise P/S	Yes	1	No	-	1
12	P/S impedance 1400 Ω	No	-	Yes	Patient Alert	1
13	Noise P/S	Yes	25	No	-	1
14	Noise P/S	Yes	Unknown	No	-	1
15	Intermittently capture of P/S	No	-	No	-	1
16	P/S impedance 2208 Ω	No	-	Yes	Patient Alert	1
17	Defibrillator conductor impedance > 200 Ω	No	-	Yes	Patient Alert	1
18	Noise P/S	Yes	14	No	-	1
19	SIC >3000	No	-	No	-	1
20	Noise P/S	No	-	Yes	LIA	1+2
21	Noise P/S	Yes	13	Yes	LIA	1+2
22	Noise P/S	No	-	Yes	LIA	1+2
23	Noise P/S	No	-	Yes	LIA	1+2

P/S = Pace-sense conductor; SIC = Sensing Integrity Counter; IAS = Inappropriate Shocks due to lead failure; LIA = Lead Integrity Algorithm;

device follow-up and the remaining 4 cases were detected by the RV-impedance Patient Alert™.

For implementation of the second advisory, 299 patients were invited of which 297 patients attended. LIA was uploaded into all software compatible ICDs (n=254, 86%). Devices of the Marquis (n=41, 13%) and Consulta (n=2, 1%) family were at that time software incompatible. In January 2009, the newer version of LIA was uploaded in all ICDs

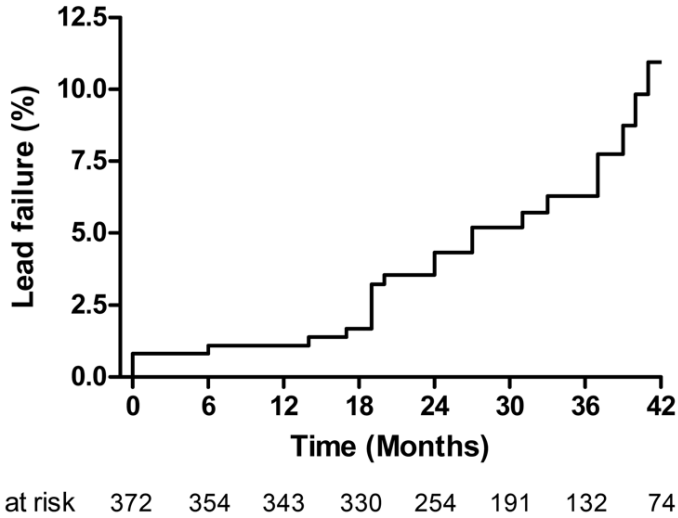

Figure 2. Kaplan Meier curve for Sprint Fidelis lead failure

of the Marquis family. Hence, LIA was uploadable in 99% of all devices by January 2009. Assessment of the alert audibility revealed that 18 patients (6%) were unable to hear the alert.

Remote monitoring was offered to all 297 patients of whom 93% (n=275) accepted its use. Causes of refusal were inaccessibility to a fixed telephone network (n=14, 4%), fear of constant confrontation with the ICD (n=6, 2%) or living abroad (n=2, 1%). Of the 275 patients who received a monitor, 231 (84%) patients were able to perform a test transmission at home. The majority of installation problems were related to non-analogue telephone lines (54%).

Period C

During the period following the 2nd advisory, 1 patient (<1%) died and 5 SF leads (2%) were removed. Four of these removals were due to lead failure and 1 was prophylactically replaced during ICD replacement. LIA was triggered in all cases of lead failure. However, as can be noted in table 2, one patient received inappropriate shocks regardless of the LIA warning, which was triggered only 5 minutes before the occurrence of inappropriate device discharges.

Effect of advisories

During complete follow-up (period A, B and C) of 923 lead-years, a total of 23 cases of lead failure were identified of which 12 patients presented with inappropriate shocks. The cumulative incidence of lead failure was 3.6% [95%CI 1.6 – 5.6] at 21 months and increased to 11.0% [95%CI 6.1 – 15.9] at 42 months. As can be seen in Figure 2, the

Table 3. Inappropriate shocks per period

Period	Total lead-years	Cases of IAS (n)	Cases of IAS/100 lead-years (CI 95%)
A	481	7	1.5 [0.59, 3.00]
B	311	4	1.3 [0.35, 3.29]
C	131	1	0.8 [0.02, 4.25]
Total	923	12	1.3 [0.67, 2.27]

IAS = Inappropriate shocks due to lead failure

cumulative incidence of lead failure appeared to accelerate over time. The rate of inappropriate shocks per lead failure decreased from 78% (7 out of 9 patients) to 25% (1 out of 4 patients) after implementing both advisories. Differentiation by the pre-defined periods revealed an event rate of inappropriate shocks per 100 lead-years of 1.5 [95% CI 0.59, 3.00] in period A, 1.3 [95% CI 0.35, 3.29] in period B and 0.8 [95% CI 0.02, 4.25] in period C (Table 3). Noteworthy, in every patient with an adverse event, the advisory, prior to that event, was implemented.

Non-Medtronic devices

In 18 cases (5%), the implanted ICD was not manufactured by Medtronic, which made it impossible to fully comply with the safety advisories. However, all patients were seen at the outpatient clinic every 3 months after the first advisory. During follow-up, 3 leads (17%) (all combined with an ICD by Biotronik) were removed, of which 2 cases (11%) were identified as lead failure. In addition, both cases of lead failure caused noise on the electrogram and subsequently multiple inappropriate shocks.

Discussion

To comply with the safety advisories of Medtronic we conducted two clinical evaluations and presented the results of these recommendations in daily practice. The major findings of the current study can be summarized as follows: 1) the cumulative incidence of SF lead failure increased from 3.6% at 21 months to 11% at 42 months; 2) implementation of both advisories reduced the occurrence of inappropriate shocks due to lead failure from 1.5 to 0.8 per 100 lead-years; 3) all advisories were easily conducted in most patients.

Device alerts

The ICD lead has frequently been described as the weakest link of the ICD system, being most vulnerable to failure.[4] Taken in consideration that failure of this lead might render the system incapable of responding adequately in case of a life threatening arrhythmia, timely detection is desirable to maximize patient safety. Becker et al. reported that standard

impedance-measurement-based patient alerts in ICDs are useful additional tools for early detection of lead failure.[12] However, these impedance measurements alone seemed to be insufficient for inappropriate therapy prevention.[13, 14] Accordingly, the research focus shifted to the combined use of impedance measurements with quantitative measures of oversensing resulting in a better and earlier lead failure detection.[15, 16] Swerdlow and co-workers developed an uploadable algorithm based on a nonphysiologically short R-R interval detection, the sensing integrity counter and the nonsustained tachycardia log.[17] In their retrospective analysis, this LIA improved advance warning of lead failure and, consequently, Medtronic advised installation of LIA in all Medtronic devices with a SF lead.[10] The current, prospective analysis demonstrates that LIA can be uploaded in 99% of the Medtronic ICDs and its effect on the occurrence inappropriate shocks due to lead failure seems promising. Specifically, after implementation of LIA, all cases of lead failure were preceded by a LIA alert. Unfortunately, in one patient, it was triggered only 5 minutes before 13 inappropriate device discharges. Nevertheless, the rate of patients receiving inappropriate shocks due to lead failure diminished from 1.5/100 lead-years to 0.8/100 lead-years after implementation of both advisories. Taken into account the results of the current analysis, LIA seems to be the most promising recommendation for reducing inappropriate device discharges due to failure of the SF lead.

However, LIA is only uploadable in ICDs by Medtronic. Five percent (n=18) of the patients, implanted with a SF lead at our hospital, could not benefit for the advisories of Medtronic since a non-Medtronic ICD was implanted. Thus far, 2 patients experienced inappropriate shocks due to lead failure but the remaining 16 patients are still at risk for adverse events caused by lead failure. It is implausible that manufacturers, other than Medtronic, will address this issue with a Medtronic lead. To comply with future advisories and to maximize patient safety, it may be advisable to implant leads and pulse generator by the same manufacturer in most patients.

In the general ICD treated population, Kleemann et al reported inappropriate shocks secondary to lead failure in 33% of patients.[3] Although this percentage is significantly lower than observed in period A of the current study (78%), a beneficial effect of changing ICD programming similar to the SF advisories, might be achieved in patients with leads, other than SF. The current study assessed several methods for prevention of these adverse events and so far, the combination of lower lead impedance alerts and LIA seems to be the most promising way to improve early diagnosis of lead failures. In line with these results, it may be advisable for device manufactures to investigate the optimal lead impedance thresholds and the possibility to implement LIA or LIA-like software into all ICDs, regardless of the lead performance.

Future perspectives

In case of a device alert, rapid response and quick analysis are warranted for several reasons. Firstly, besides LIA, every ICD by Medtronic is equipped with 6 other audible patient-alerts representing different urgencies and requiring different treatment strategies.[12] Secondly, the interval between indicators of lead failure and the first occurrence of inappropriate shocks is short; often only hours to days.[17] However, in daily practice, these audible alerts appeared to be insensitive with an average time from audible alert to ICD interrogation of 5.3 days. Moreover, 5 patients reported having heard an audible alarm without documented event in the device memory.[18] To address these limitations, remote monitoring seems an appropriate answer, facilitating quick remote access to the device information. In addition, the latest devices can automatically transmit a wireless remote monitoring alert to notify the physician. In the current study, only one patient used remote monitoring in response to a LIA-alert, resulting in timely identification of lead failure and consequent lead replacement. Nonetheless, remote monitoring might pose to be a safe and efficient means for ICD follow-up.

Limitations

Although all ICDs and leads are periodically screened for integrity and adequate function, some cases of lead failure might occur without clinical symptoms or alerts, causing them to go unnoticed. This will eventually lead to an underestimation of the actual incidence of lead failure and an overestimation of the percentage of lead failures presented with adverse events. Furthermore, the current study demonstrated a strong decrease of inappropriate shocks due to lead failure which seemed to be the result of the advisory implementation, but other explanations are conceivable, including increase of alertness by patient and physician. However, even greater awareness can be considered as a positive effect of these advisories.

Conclusion

The current study demonstrates that despite an increasing risk for SF lead failure, implementation of SF lead advisories decreased the occurrence of inappropriate shocks due to lead failure. Of these advisories, LIA seems to be the most effective in the prevention of inappropriate device discharges by alerting 75% of all patients prior to the occurrence. These findings imply the beneficial effect of the advisories on patient safety.

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