Inappropriate interventions during the long-term follow-up of patients with an implantable defibrillator

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Summary

Questions under study: In patients with an implantable defibrillator (ICD), inappropriate ICD interventions alter the quality of life, may cause hospitalisations and limit cost-effectiveness. The aim of the study was to determine the incidence and causes of inappropriate ICD interventions, and to identify patients at risk.

Methods: For this observational longitudinal study, consecutive patients undergoing ICD implantation at the University Hospital of Berne were included in a registry. All stored electrograms of episodes triggering ICD interventions were systematically reviewed and analysed to determine whether ICD interventions were appropriate or inappropriate. Inappropriate ICD interventions were classified according to their cause, and risk factors were sought.

Results: 214 consecutive patients were followed during a median time of 2.7 years (3.7 years IQR, 698 patient years). 81 inappropriate ICD interventions occurred in 58 patients (27%). Factors trig-gering inappropriate ICD interventions included atrial fibrillation and flutter (n = 35, 44%), sinus tachycardia (n = 26, 32%), lead fracture (n = 12), recurrent self-terminating ventricular tachycardia (n = 5), double-counting due to T-wave oversens-ing (n = 3). The only identifiable risk factor for inappropriate ICD interventions was sustained ventricular tachycardia as index arrhythmia.

Conclusions: An important proportion of ICD patients suffer inappropriate ICD interventions that are most commonly due to supraventricular arrhythmias. Patients with ventricular tachycardia prior to ICD implantation are at higher risk of inappropriate ICD interventions. Interventions aiming at decreasing the risk of inappropriate ICD interventions should be considered in these patients.

Key words: implantable cardioverter defibrillator; adverse event; inappropriate shock

Introduction

Multiple studies have established the implantable cardioverter defibrillator (ICD) as an efficient therapy for primary and secondary prevention of sudden cardiac death [1, 2]. However, several complications can affect ICD patients during the long-term follow-up. Among them, inappropriate ICD interventions with unnecessary over-drive-pacing or electrical shocks can cause psychological distress, particularly after multiple shock applications. Furthermore, inappropriate ICD interventions can necessitate hospitalisation, reduce ICD battery longevity, and reduce cost-effectiveness of ICD treatment. Finally, there have been some reports of ventricular arrhythmias induced by inappropriate ICD interventions that may be life-threatening. In the AVID study 17% off all device interventions were inappropriate [3]. Young patients and those patients with a history of atrial arrhythmias are known to be at risk according to

previous study, and a dual-chamber ICD is usually selected for these patients, to better identify recurrent supraventricular arrhythmias [4–8]. Detection enhancement algorithms enable dual-chamber ICDs to correctly identify up to 95% of all supraventricular tachycardias (SVT) [9, 10]. However, dual-chamber ICDs are not routinely used in other patients, in order to limit the material implanted and to decrease ventricular pacing, which desynchronises left ventricular contraction and increases the incidence of heart failure [11].

In view of the rapidly growing population of ICD patients, it appears important to focus on

List of abbreviations

ICD	=	implantable cardioverter defibrillator
VT	=	ventricular tachycardia
SVT	=	supraventricular tachycardia

adverse events that may alter patients' quality of life and limit cost-effectiveness of the treatment. Analysis of the characteristics and the causes of inappropriate ICD interventions are needed for the development of strategies aiming to prevent these adverse events.

Accordingly, the study was performed to analyse the incidence and causes of inappropriate ICD interventions during long-term follow-up in a group of consecutive ICD recipients, as well as to identify the patients at risk to present with inappropriate ICD interventions.

Methods

Consecutive patients that received an ICD between January 1995 and December 2002 were included in a database. A retrospective analysis of the database was performed. All patients had biannual routine ICD controls and additional ICD interrogations in case of interventions. All devices were capable to store electrocardiograms for analysis of the arrhythmias triggering ICD interventions. All stored arrhythmias and ICD interventions were reviewed by a senior electrophysiologist to determine the nature of arrhythmias, as well as whether device interventions were appropriate or inappropriate. After ICD implantation, device programming was performed according to the following recommendations. The detection threshold for VT was set at a rate 15 to 20 beats/min below the rate of the slowest clinically observed VT. In patients without VT prior to ICD implantation, the detection threshold was set between 180 and 200 beats/min. Detection enhancements to prevent inappropriate shocks due to supraventricular arrhythmia were programmed "on". ICD from three manufacturers (Medtronic Inc, Minneapolis, MN; Guidant Inc, Minneapolis, MN; St. Jude Medical, Sunnyvale, Ca) were implanted.
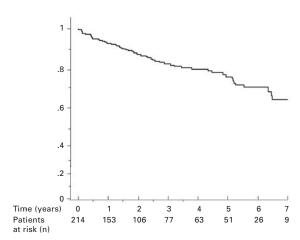
Study design

All patients were included in a registry including clinical information and ICD related characteristics that were updated on a regular basis. Inappropriate ICD intervention was considered the outcome variable. The incidence, cause and management of inappropriate ICD interventions were analysed.

Statistical analysis

Results are expressed as median (interquartile range, IQR). Estimates of survival free of inappropriate ICD therapies were analysed by the method of Kaplan and Meier. Patients' data were censored at the time of death, heart transplantation or last follow-up. We further used the method of Kaplan and Meier to analyse differences in the occurrence of inappropriate ICD interventions according to the presence or absence of the following possible risk factors: young age, SVT prior to ICD implantation, VT as index arrhythmia prior to ICD implantation (versus ventricular fibrillation or syncope as index arrhythmia, as well as ICD for primary prophylaxis), single-chamber ICD (versus dual-chamber ICD), NYHA functional class I (vs II and III), low left ventricular ejection fraction (<40% vs >40%). All analyses were done with Statview 4.5 (Abacus Concepts Inc.) and SAS 9.1 for Windows (SAS Institute Inc., Cary, NC 27513-2414, USA).

Results

Of 216 patients receiving an ICD between 1995 and 2002, 2 patients were lost to follow-up because they moved abroad, and 214 were included in the study. They were followed for a median of 2.7 years (IQR 3.7 years, 698 patient-years); 23 patients died and 11 underwent heart transplantation. Survival was 84% at 5 years of follow-up. During the follow-up, 105 of 214 patients (49%)

experienced at least one appropriate ICD intervention.

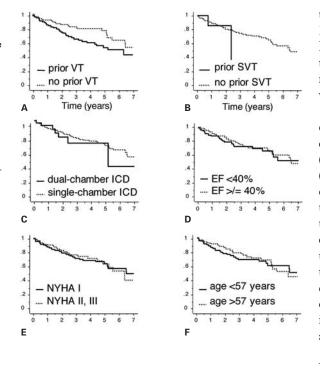### Inappropriate ICD interventions

58 patients (27%) suffered 81 inappropriate ICD interventions. 48 patients had only one episode and 10 patients had two or more inappropriate ICD interventions. Survival free of inappropriate ICD interventions is shown in figure 1. The characteristics of the patients with and without inappropriate ICD interventions are shown in table 1. Age and underlying cardiac diseases were similar in both groups. Patients with known SVT prior to ICD implantations and dual-chamber ICD were few in both groups. The proportion of patients who had received their ICD post-event (91% vs 78%) was larger in the group with inappropriate ICD interventions. Similarly the proportion of patients with VT as index-event leading to ICD implantation was larger in the group of patients who suffered inappropriate ICD interventions (64% vs 52%). Accordingly, the incidence of inappropriate ICD interventions appears higher

Figure 1

Kaplan-Meier estimates of survival free of inappropriate defibrillator intervention.

Time (years)	0	1	2	3	4	5	6	7
Patients at risk (n)	214	153	106	77	63	51	26	9

Figure 2

Kaplan-Meier estimates of survival free of inappropriate defibrillator intervention (IRx) according to following subgroups: **A**: patients with versus without ventricular tachycardia (VT) as index arrhythmia, **B**: patients with versus without known supraventricular tachycardia (SVT) prior to ICD-Implantation, **C**: patients with dual-chamber versus single-chamber ICD, **D**: patients with left ventricular ejection fraction (EF) lower than 40% versus higher than 40%, **E**: NYHA functional class I patients versus NYHA class II and III patients, **F**: patients younger versus patients older than 57 years.

in the group with VT as index arrhythmia (figure 2).

27 inappropriate ICD interventions (33%) consisted of 1.0 (2.0 IQR) overdrive pacing episode without shocks. 54 Inappropriate ICD interventions (67%) included at least one shock, with a median of 2, IQR of 4, and a maximum of 96 shocks. Most inappropriate ICD interventions were caused by supraventricular tachyarrhythmias (n = 61, 76%), including atrial fibrillation and flut-

ter (n = 35, 44%) and sinus tachycardia (n = 26, 32%); other frequent reasons for inappropriate ICD interventions were lead fracture with detection of noise (n = 12, 15%), recurrent self-terminating VT (n = 5, 6%) and T-wave oversensing with double-counting (n = 3, 4%, figures 3 and 4).

Prevention of recurrence included changes in detection parameters for 36 episodes (44%), changes in anti-arrhythmic therapy for 21 episodes (25%), ICD electrode revision in 14 episodes (17%), and ICD revision in 1 patient (1%). For 6 episodes (7%) there was deliberately no intervention undertaken (figure 4). Changes in ICD settings made after inappropriate therapy included changes in the detection rate, changes in ventricular electrode sensing, and changes in the diagnostic enhancements to prevent inappropriate shocks due to SVT. These included changes in the sudden onset cut-off value, changes in the interval stability cut-off value, and changes in the morphology analysis parameters.

Recurrences

After a first inappropriate ICD intervention, 58 patients were followed during a median of 1.46 years (2.83 years IQR, 117 patient-years). Nine additional inappropriate ICD interventions occurred before the first episode was detected at the clinical control and therefore were not counted as recurrence. A total of 10 patients (17%) had 14 recurrent inappropriate ICD interventions, but only 4 of the 58 patients (7%) had 5 inappropriate ICD interventions triggered by the same cause as the initial episode.

Table 1

Characteristics of patients with and without inappropriate ICD interventions (IRx).

	with IRx	without IRx
n	58	156
age, years	53 (16)	54 (14)
female, %	19	12
SVT prior to ICD implantation, %	3	4
Cardiac disease, %		
Ischaemic heart disease	60	61
Dilative cardiomyopathy	14	15
ARVC	5	4
Hypertrophic cardiomyopathy	0	5
other / unknown	21	15
Implantation, %		
Pre-event (primary prophylaxis of SCD)	9	22*
Post-event	91	78
Index-arrhythmia in patients with ICD post-event, %		
Ventricular tachycardia	64	52*
Ventricular fibrillation	21	27
Syncope	15	20
Dual-chamber ICD, %	12	14

Values are mean (standard deviation) or percentage of patients
IRx: inappropriate defibrillator intervention; SVT: supraventricular tachycardia;
ICD: implantable cardioverter-defibrillator; ARVC: arrhythmogenic right ventricular cardiomyopathy;
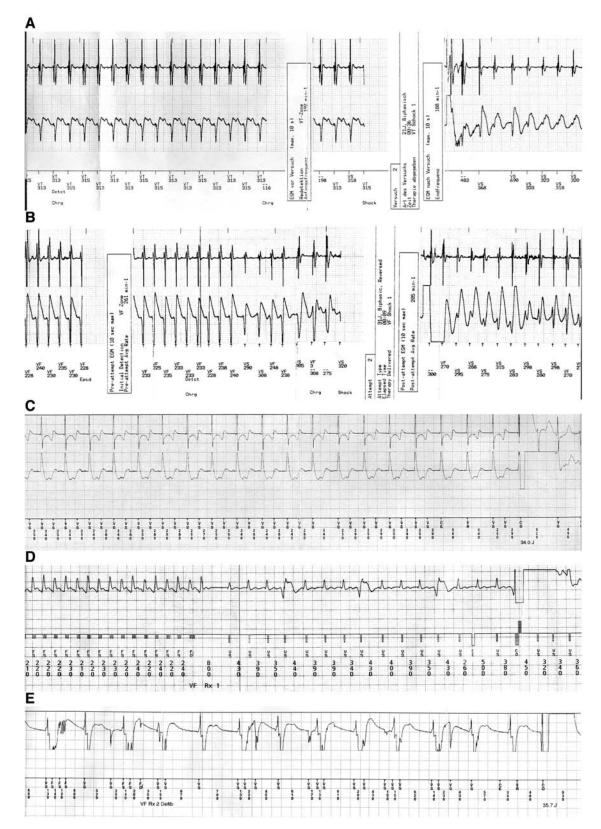* important difference

Figure 3

Several causes of inappropriate interventions: **A:** Sinus tachycardia at a rate of 190/min during a soccer game triggering inappropriate shock in a 19 y.o. patient with Fallot tetralogy who had had ICD implantation because of recurrent monomorphic VT at a rate of 190/min. Because of the progressive rate acceleration, the tachycardia was recognised as sinus tachycardia by the ICD, and therapy was initially inhibited. However, there was a time-out period of 3 minutes for treatment inhibition and therapy was resumed after 3 minutes as sinus tachycardia persisted. Treatment inhibition time-out period was subsequently increased to 15 minutes. **B:** Rapid atrial fibrillation with slightly irregular rhythm (RR intervals between 233 and 308 msec detected in the ventricular fibrillation (VF) zone, triggering high-energy shock. The shock fails to convert atrial fibrillation which was responsible for repeated shocks. Changes in the detection enhancement parameters (changes in RR stability cut-off) in a newly programmed ventricular tachycardia zone may allow preventing the inappropriate ICD intervention, but in this case, anti-arrhythmic drug therapy was necessary to slow atrial fibrillation and deemed safer to avoid further inappropriate ICD shocks. **C:** T wave oversensing with double-counting and inappropriate detection in the ventricular tachycardia zone leading to a 34 Joule-shock (subsequent to unsuccessful overdrive pacing attempts, not shown). The problem could be solved by decreasing the sensitivity (sensing threshold at 0.6 mV instead of 0.3 mV). In some other situations, the ICD lead needs to be repositioned or changed. **D:** Non-sustained, rapid ventricular tachycardia (cycle length 230 msec) detected by the ICD just before spontaneous termination. ICDs of the new generation perform redetection of the arrhythmia at the end of the charging time (CE) before energy delivery (CD), which may prevent inappropriate ICD intervention in this situation. Anti-arrhythmic drug therapy preventing longer VT runs or prolongation of the VT detection time can also efficiently prevent further inappropriate ICD interventions. **E:** Lead rupture with electrical artefacts (noise) detected in the ventricular fibrillation zone, responsible for repeated high-energy shocks. A new ICD lead was implanted.
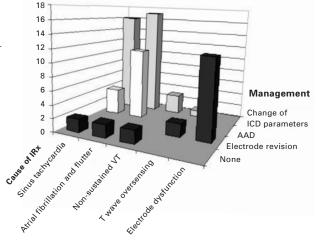
Discussion

Whereas ICD trials have mainly focused on the benefits conferred by device therapy, information available about adverse events is scant. The present study demonstrates that inappropriate ICD interventions were frequent, affecting a quarter of the patients within a 3-year follow-up. The majority of inappropriate ICD interventions included repeated electrical shocks, which alter patients' quality of life. Moreover, inappropriate ICD interventions often necessitated hospitalisations, additional procedures, and outpatient visits that may limit the cost-effectiveness of the therapy and that were not integrated in previous analyses [12]. In a similar study by Teusch et al. 14% of the patients experienced inappropriate ICD interventions during a 22-month follow-up. However, only inappropriate ICD interventions due to SVT were reported. In our study, there were additional causes of inappropriate ICD interventions including electrode dysfunction, due to the rupture of one of the coils, T wave oversensing with double-counting and repeated self-terminating VT.

Three out of four inappropriate ICD interventions were triggered by SVTs. Analysis of the tachycardia (abrupt or slow heart rate increase) and of the RR interval stability, as well as QRS morphology analyses are detection enhancements that often, but not always, allow to recognise SVT and prevent inappropriate ICD interventions. Since SVT detection algorithms sometimes fail to prevent inappropriate ICD interventions, optimisation of the programmed parameters on an individual base is sometimes needed and additional detection enhancements are desirable. Friedman et al. recently showed that dual-chamber detection enhancements improve the recognition of SVT and decrease the rate of inappropriate therapy from 39.5% to 30.9% when compared to single-chamber, ventricular only detection enhancements [4]. In our collective, dual-chamber ICDs were used in

a minority of the patients (13%) who needed permanent pacing. Indeed, it is common practice to avoid the implantation of multiple electrodes in ICD recipients, first to decrease implanted material in relatively young patients and second because ventricular stimulation in the DDD pacing mode may exacerbate heart failure [11]. However, the recent study by Friedman, together with the availability of dual chamber ICD systems allowing minimising ventricular pacing and desynchronisation, should foster the use of dual-chamber ICD rather than single-chamber ICD, at least in the population at risk to develop inappropriate ICD interventions.

Some subgroups of patients are at greater risk to develop inappropriate ICD interventions. Patients with VT as index-arrhythmia prompting ICD implantation appear at higher risk to suffer inappropriate ICD interventions (figure 2). In these patients, VT detection rate cut-off are recommended to be set 15–20 beats/min lower than VT rate and may be as low as 150 or 160/min. With low detection rate, rapid atrial fibrillation or sinus tachycardia can be misinterpreted as VT. In the study by Theuns et al., patients with slow VT (171/min and lower) were also found at risk to suffer inappropriate ICD interventions. Implantation of a dual chamber ICD to optimise detection enhancements should be considered with sustained VT. However, since dual-chamber detection enhancements could only decrease inappropriate ICD interventions from 39.5% to 30.9%, studies analysing the role of catheter ablation of ventricular tachycardia to decrease inappropriate ICD interventions in the group of patients at risk would be of special interest.

In the patients analysed by Theuns et al., the major risk factor was a history of SVT. Intriguingly, 29% of the relatively young patients studied (on average 60 years old) had a history of SVT, compared to 4% in our population of similar age and to 8% in the MADIT II study, including older patients (on average 65 years old). This suggests that their definition of a "history of SVT" was unusual or biased, ie including nonsustained atrial tachycardias, sinus tachycardia above a certain rate, or more probably tachyarrhythmias at any time of the follow-up. Generally, a history of SVT prior to ICD implantation prompts very careful ICD parameter programming or/and antiarrhythmic drug therapy, but in our experience, the problem is uncommon. The difficulties most often encountered are related to patients who unexpectedly develop rapid atrial fibrillation after ICD implantation or are related to the younger, physically very active, patients with sinus tachycardia above 150 or 160/min.

Of the 58 patients with inappropriate ICD interventions, 10 patients (17%) had 14 recurrent in-

Figure 4

Number of episodes of inappropriate defibrillator interventions (IRx) according to their cause, and subsequent management of the adverse event; ICD, implantable cardioverter-defibrillator; VT, ventricular tachycardia; AAD, antiarrhythmic drug therapy.

appropriate ICD interventions. Only 4 of the 58 patients (7%) had inappropriate ICD interventions triggered by the same cause as the initial episode. This demonstrates that the management of the problem, aiming to prevent further inappropriate ICD interventions, was successful in most cases.

Limitations

An association between a lower rate cut-off for VT detection and a higher risk of inappropriate ICD interventions cannot be inferred from our data. The analysis of the influence of detection parameters (ie rate cut-off and detection enhancements) on the incidence of inappropriate ICD interventions would require a study design prohibiting any change in these parameters and with a fixed follow-up time for each patient.

The data allowed to explore the conditions associated with a higher incidence of inappropriate ICD interventions. However, the statistical power of the study was insufficient to demonstrate that covariates were independently associated with a risk of inappropriate ICD interventions (there are several covariates plausibly associated with inappropriate ICD interventions and the number of events was relatively small).

Conclusion

Inappropriate ICD interventions are common adverse events in the long-term follow-up of ICD patients. They are most commonly triggered by SVT. Patients with sustained VT as index-event prompting ICD implantation seem at higher risk to suffer inappropriate ICD interventions and may benefit from strategies aiming to improve the detection of SVT or to abolish VT.

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