

Role of medical reaction in management of inappropriate ventricular arrhythmia diagnosis: the inappropriate Therapy and HOme monitoRiNg (THORN) registry

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Aims

Implantable cardioverter-defibrillators (ICDs) reduce sudden cardiac death in selected patients but inappropriate ICD shocks have been associated with increased mortality. The THORN registry aims to describe the rate of inappropriate ventricular arrhythmia diagnoses and therapies in patients followed by remote monitoring, as well as the following delay to next patient contact (DNPC).

Methods and results

One thousand eight hundred and eighty-two patients issued from a large remote monitoring database first implanted with an ICD for primary or secondary prevention in 110 French hospitals from 2007 to 2014 constitute the THORN population. Among them, 504 patients were additionally followed prospectively for evaluation of the DNPC. Eight hundred and ninety-five out of 1551 (58%) patients had ischaemic heart disease and 358/771 (46%) were implanted for secondary prevention. During 13.7 ± 3.4 months of follow-up, the prevalence of first inappropriate diagnosis in a ventricular arrhythmia zone with enabled therapy was 162/1882 (9%). Among those patients, 122/162 (75%) suffered at least one inappropriate therapy and 58/162 (36%) at least one inappropriate shock. Eighty-three out of 162 (51%) of first inappropriate diagnosis occurred during the first 4 months following implantation. The median DNPC was 8 days (interquartile range 1–26). At least one other day with recording of an inappropriate diagnosis of the same cause occurred in 13/43 (30%) of available DNPC periods, with an inappropriate therapy in 7/13 (54%).

Conclusion

Inappropriate diagnoses occurred in 9% of patients implanted with an ICD during the first 14 months. The DNPC after inadequate ventricular arrhythmia diagnoses remains long in daily practice and should be optimized.

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Identifier

Keywords

Implantable cardioverter-defibrillator • Inappropriate implantable cardioverter-defibrillator shock • Inappropriate implantable cardioverter-defibrillator therapy • Inappropriate ventricular arrhythmia diagnosis • Medical reaction time • Remote monitoring

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What's new?

- Inappropriate ventricular diagnoses by implantable cardioverter-defibrillator (ICD) remain frequent, occurring in 9% of patients first implanted with an ICD device for primary or secondary prevention at 13.7 months follow-up.
- However, the rate of inappropriate shock is low (3%) in patients followed by remote monitoring (RM), most probably due to corrective actions.
- Despite the median delay from the inappropriate diagnosis to the confirmation on the RM platform was 1 day, the median delay to next patient contact remained 8.0 days long in our population.
- Prompt and adequate corrective action is critical, as at least one other day with recording of an inappropriate diagnosis occurred in 30% of medical reaction periods, with an inappropriate therapy in more than half of those recurrences.
- There is a correlation between the duration of the delay to next patient contact and the risk of recurrence of inappropriate diagnoses before the corrective action occurs.

Introduction

Implantation of implantable cardioverter-defibrillators (ICDs) reduces sudden cardiac death (SCD) in selected patients suffering from ischaemic as well as non-ischaemic heart diseases.^{1–3} On the other hand, inappropriate ICD shocks have been associated with increased mortality.⁴ In the last years, several studies have demonstrated that increasing the heart rate limit triggering ICD therapy and prolonging the duration of the detection window before therapy delivery may reduce inappropriate therapies and remain safe.^{5–8} However, inappropriate ICD therapies resulting from detection of intracardiac or extracardiac signals still occur in around 5% patients at 1.5 years.⁵ On a different note, remote monitoring (RM) has also been proven to reduce the rate of inappropriate shocks⁹ and even mortality.¹⁰

The present observational registry aims to evaluate (i) the prevalence of inappropriate diagnoses and inappropriate therapies in primary and secondary prevention patients followed by RM, as well as (ii) the delay to the next patient contact (DNPC) and its correlation with potential recurrences.

Methods

Design and patients

The THORN population is issued from a large database regrouping patients first implanted between 2007 and 2014 in 110 French hospitals with a Biotronik ICD with enabled RM function (Lumax[®] family). No restriction concerning underlying cardiomyopathy or indication for the ICD implantation (primary prevention or secondary prevention) was made. Paediatric patients (age <18 years), as well as patients in New York Heart Association heart failure functional Class IV and with leads under recall were excluded from analysis.

All patients implanted from March 2012 to September 2013 in 56 hospitals were on top of being included in the THORN population also followed prospectively, in order to collect specific data concerning DNPC and recurrence thereafter.

The implantation strategy as well as the programming of the devices, including parameters of RM transmissions, were left to the discretion of the treating electrophysiologists. All participating centres followed the international standards of cardiology practice^{11,12} and updated recommendations for optimizing detection of ventricular tachycardia (VT) and ventricular fibrillation (VF) were provided to guide physicians, including activation of supraventricular tachycardia (SVT) discriminators.

The follow-up (FU) started at hospital discharge, with a target of 15 months. All patients were seen for routine FU according to current good-practice guidelines for RM, which consist of a remote interrogation or an in-office visit every 3–6 months, with a least one in-office visit every year.¹¹ Additional in-office FU could be triggered following a RM event notification or according to the patients or clinicians needs.

The registry complies with the ethical guidelines of the 1975 Declaration of Helsinki and the protocol was reviewed and approved by the relevant Ethics Committees. All patients gave written informed consent allowing the use of their medical data.

Remote monitoring features

All patients were equipped with the routine RM transmitter of their device, which is an internet-based system capable of automatic daily data transmission of device parameters (sensing amplitudes, lead impedances, battery capacity, counters) and of stored intracardiac electrograms (Home Monitoring[®], Biotronik, Germany). The data are transmitted via the Global System for Mobile communication network to the Home Monitoring Service Center and the physicians were automatically informed via email. As per routine FU, the data received by the Service Center could be viewed by the physicians via a secured website. The frequency of control of the notifications was left to the discretion of the treating electrophysiologists. Remote monitoring was activated and functional from hospital discharge in all patients. The date of assessment of the transmitted notifications was registered on the RM platform.

Data gathering and analysis

All transmitted VT/VF electrograms (EGMs) from the THORN population were reviewed retrospectively by an adjudication committee (see Appendix) blinded to clinical information. Each EGM was classified as appropriate VT/VF in case of real ventricular arrhythmia, inappropriate VT/VF if the stored VT/VF episode was due to another cause than ventricular arrhythmia, or undeterminate. Only inappropriate diagnoses that occurred in a ventricular arrhythmia zone with enabled therapy were considered for analysis. Further, in the event of an inappropriate diagnosis, the EGM could eventually be classified on top as inappropriate VT/VF diagnosis with therapy [antitachycardia pacing (ATP) and/or shock]. Finally, the inappropriate diagnosis cause was specified, including SVT or oversensing [T-wave oversensing, R-wave double counting, or noise (electromagnetic or lead-related interferences)].

For the prospective subgroup, an electrophysiologist was in charge of the FU controls of the enrolled patients in every participating centre. For each inappropriate episode classified as VT or VF, the physician had to report prospectively information about the event, including date, delivered therapies as ATP or shock, inappropriate diagnosis cause, the corrective action taken (including its date), and the number of days with recurrences of at least one inappropriate diagnosis of the same cause until the end of the DNPC.

Endpoints

THORN population

We addressed retrospectively (i) the prevalence of patients experiencing at least one inappropriate diagnosis, at least one inappropriate therapy or at least one inappropriate shock during FU, (ii) the inappropriate diagnosis cause, as well as (iii) the data transmission rate, calculated as the number of days during which data were transmitted by the RM system divided by the number of FU days. Only the first inappropriate diagnosis, inappropriate therapy or inappropriate shock were considered for analysis during FU in each patient.

Prospective subgroup

The specific information collected in this subpopulation were (i) the DNPC: total time delay from the inappropriate diagnosis to the next patient contact (inpatient FU, hospitalization, or phone call), including the delays from the inappropriate diagnosis to notification transmission, from notification transmission to confirmation of the notification on the RM platform, and from confirmation to first clinical contact, (ii) the proportion of patients with at least one recurrence of an inappropriate diagnosis or therapy of the same cause within the DNPC (intra-DNPC recurrence), (iii) the proportion of patients with at least one recurrence of an inappropriate diagnosis or therapy of the same cause after the corrective action (post-DNPC recurrence), (iv) the total number of hospitalizations/deaths related to inappropriate diagnosis or therapy, and (v) the all-cause mortality. All DNPC periods from the available FU were considered for analysis.

Statistical analysis

This report is prepared in compliance with the STROBE checklist for observational studies.¹³ The distribution of all variables was verified with the Shapiro–Wilk test. Continuous variables are presented as means [standard deviation (SD)] or median [interquartile range (IQR)] and compared by using a Student's *t*-test or a non-parametric Mann–Whitney test where appropriate. Dichotomous variables are presented as counts (%) and compared using the χ^2 or Fisher's exact test where appropriate. We calculated proportions using non-missing values. Time to first inappropriate diagnosis event and cumulative event rates have been evaluated by using Kaplan–Meier method and compared using log-rank test. Deaths were considered as censoring events. All statistical tests were performed at a $P=0.05$ significance level, using the SAS programme v9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Population

A total of 1882 patients were implanted from June 2007 to June 2014 and constitute the THORN population. Of those, 504 patients implanted from March 2012 to September 2013 constitute the prospective subgroup. Mean FU durations were 13.7 (SD: 3.4) and 14.3 (SD: 2.7) months for the THORN population and the prospective subgroup respectively.

Table 1 illustrates baseline characteristics of both cohorts at ICD implantation. In total, 850 (45%), 503 (27%), and 529 (28%) patients in the THORN population were implanted with single-chamber ICD (including 3% ventricular leads with atrial sensing ability), dual-chamber ICD, and cardiac resynchronization therapy defibrillators (CRT-D), respectively. Mean age at implantation was 62.9 (SD: 12.8) years. Significantly more patients in the THORN

population were implanted with single or dual-chamber devices for secondary prevention of SCD (46% vs. 38% in the prospective subgroup, $P<0.0001$). A total of 1666 (89%) patients had an enabled VT zone with therapy. On average, the first VT zone with therapy was set up at 173 b.p.m. (SD: 12 b.p.m.) and the VF zone at 225 b.p.m. (SD: 13 b.p.m.). The first ventricular arrhythmia zone with therapy was significantly higher in case of primary prevention (mean: 178 b.p.m., SD: 21 b.p.m.) compared with secondary prevention (mean: 168 b.p.m., SD: 23 b.p.m., $P<0.0001$). The first VT zone with therapy was significantly higher in the prospective subgroup, with a mean of 175 b.p.m. (SD: 11 b.p.m.), $P<0.0001$. No statistically difference was noted for the VF zone between the THORN population and the prospective subgroup.

On average, transmission occurred in 86% (SD: 15%) of the days of FU.

Prevalence of inappropriate diagnoses, therapies and shocks

During the available FU, 2867 EGMs registered in the VT or VF zones from 430 patients of the THORN population were transmitted by RM. After assessment by the adjudication committee, 2307 EGMs (81%), 527 EGMs (18%), and 33 EGMs (1%) were determined to be appropriate, inappropriate, and undeterminate, respectively. Of those 527 inappropriate EGMs, 142 inappropriate ventricular arrhythmia diagnoses, which occurred in 35 patients, constitute the dataset for the analyses concerning the prospective subgroup.

Figure 1 depicts the prevalence of patients with at least one inappropriate diagnosis, one inappropriate therapy, or one inappropriate shock at the end of FU. Among a total of 162 patients of the THORN population with at least one inappropriate diagnosis, 122 (75%) suffered from at least one inappropriate therapy and 58/162 (36%) from at least one inappropriate shock. There was no difference concerning the prevalence of inappropriate diagnoses, therapies or shocks, between patients implanted for primary prevention or secondary prevention. When considering the complete FU period in patients with inappropriate events, the mean number of inappropriate diagnoses, therapies, and shocks per patient was 3.1 (SD: 5.4), 2.9 (SD: 4.2), and 1.3 (SD: 0.7), respectively. Among a total of 1005 delivered shocks in the THORN population, 75 (7%) were inappropriate.

As shown in Figure 2, there was no statistical difference concerning inappropriate diagnosis causes between the THORN population and the prospective subgroup ($P=0.10$).

The median time from implantation to first inappropriate diagnosis was 116.5 (IQR 54–240) days, i.e. half of first inappropriate diagnoses (83/162, 51%) occurred within the first 4 months of FU. Similarly, 64/122 (52%) of first inappropriate therapies and 33/58 (57%) of first inappropriate shocks occurred within 4 months following implantation. Cumulative occurrence and causes of first inappropriate diagnoses during FU are represented in Figure 3. No significant difference in time to first inappropriate diagnosis was noted between SVT and oversensing ($P=0.56$). As shown in Figure 4 for the THORN population, the lower the zone with enabled therapy, the higher was the risk of experiencing an inappropriate therapy ($P=0.005$).

Table 1 Baseline characteristics

Characteristics	Prospective subgroup (N = 504)		THORN population (N = 1882)	
	Data available	N (%) or mean \pm SD	Data available	N (%) or mean \pm SD
Male	504 (100)	422 (84)	1572 (84)	1315 (84)
Age (years)	504 (100)	63.5 \pm 13.0	1567 (83)	62.6 \pm 12.8
NYHA ^a class				
I	504 (100)	97 (19)	1470 (78)	249 (17)
II	504 (100)	259 (51)	1470 (78)	748 (51)
III	504 (100)	147 (29)	1470 (78)	459 (31)
Hypertension ^b	504 (100)	176 (35)	1432 (76)	584 (41)
LVEF \leq 35%	504 (100)	377 (75)	1454 (77)	1103 (76)
Documented SVT	504 (100)	151 (30)	1524 (81)	462 (30)
Documented VT/VF	504 (100)	198 (33)	1506 (80)	621 (41)
Primary prevention ^c	363 (72.0)	227 (63)	771 (41)	413 (54)
Secondary prevention ^c	363 (72.0)	136 (38)	771 (41)	358 (46)
Ischaemic heart disease	504 (100)	286 (57)	1551 (82)	895 (58)
Myocardial infarction	504 (100)	240 (48)	1551 (82)	658 (42)
ACE inhibitors and AT receptor blockers	504 (100)	412 (82)	1001 (53)	800 (80)
Beta-blockers	504 (100)	432 (86)	1029 (55)	849 (83)
Amiodarone	504 (100)	103 (20)	1029 (55)	215 (21)
Other Antiarrhythmic	504 (100)	18 (4)	964 (51)	41 (4)
Aldosterone antagonist	504 (100)	194 (39)	964 (51)	307 (32)

Data are reported as counts (%).

ACE, angiotensin converting enzyme; AT, angiotensin II; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SD, standard deviation; SVT, supraventricular tachycardia; THORN, Therapy and HOme monitoring; VF, ventricular fibrillation; VT, ventricular tachycardia.

^aNew York Heart Association heart failure functional class.

^bHigh blood pressure.

^cInformation concerning indication was not available for patients implanted with cardiac resynchronization therapy defibrillators.

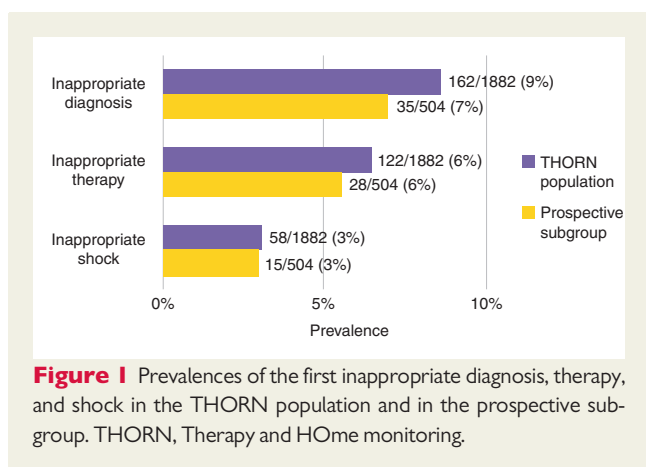


Figure 1 Prevalences of the first inappropriate diagnosis, therapy, and shock in the THORN population and in the prospective subgroup. THORN, Therapy and HOme monitoring.

Management and recurrences of inappropriate diagnoses in the prospective subgroup

Data on DNPC and the associated corrective actions were available for 43 out of 54 inappropriate diagnoses episodes, which

occurred in 28 out of 35 patients of the prospective subgroup with at least one inappropriate diagnosis. Five inappropriate diagnoses episodes were interpreted as appropriate by the treating centres and therefore no information concerning DNPC is available. For the six remaining inappropriate diagnoses, the treating electrophysiologists decided only to control more regularly the patient by RM without specific patient contact. The time delay from inappropriate diagnosis occurrence to transmission was 1 day or less in 41/43 (95%) episodes. The median delay from inappropriate diagnosis to confirmation on the RM platform was 1 day (IQR 0.0–3.0). The median DNPC was 8 days (IQR 1.0–26.0). *Figure 5* depicts the median DNPC durations according to cause, classification of the event by the device, and therapy occurrence. The median DNPC was numerically shorter in case of oversensing, classification of the event as VF or treatment delivery.

At least one other day with recording of an inappropriate diagnosis of the same cause occurred in 13/43 (30%) of available DNPC periods, with an inappropriate therapy in 7/13 (54%). There was a significant difference between the duration of DNPC and the presence or not of intra-DNPC recurrence [median of 20 days (IQR 11–33) vs. 3.0 days (IQR 1–16), respectively, $P = 0.01$].

Table 2 summarizes the management of the first inappropriate diagnosis for the patients of the prospective subgroup. Thereafter, 9/35

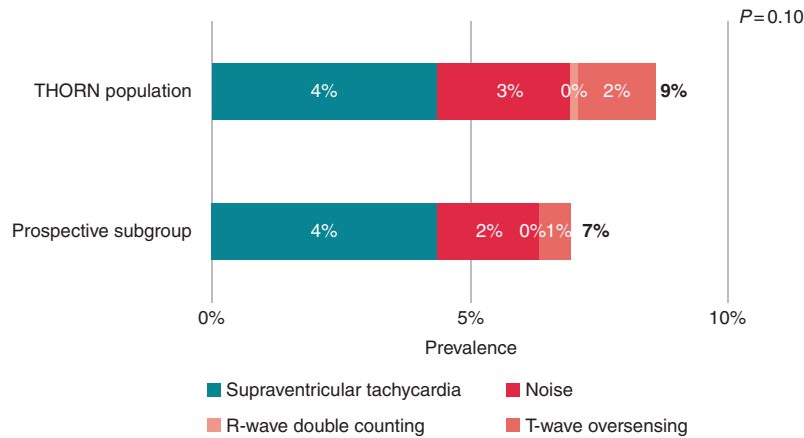


Figure 2 Causes of the first inappropriate diagnosis in the THORN population and in the prospective subgroup. THORN, Therapy and HOme monitoring.

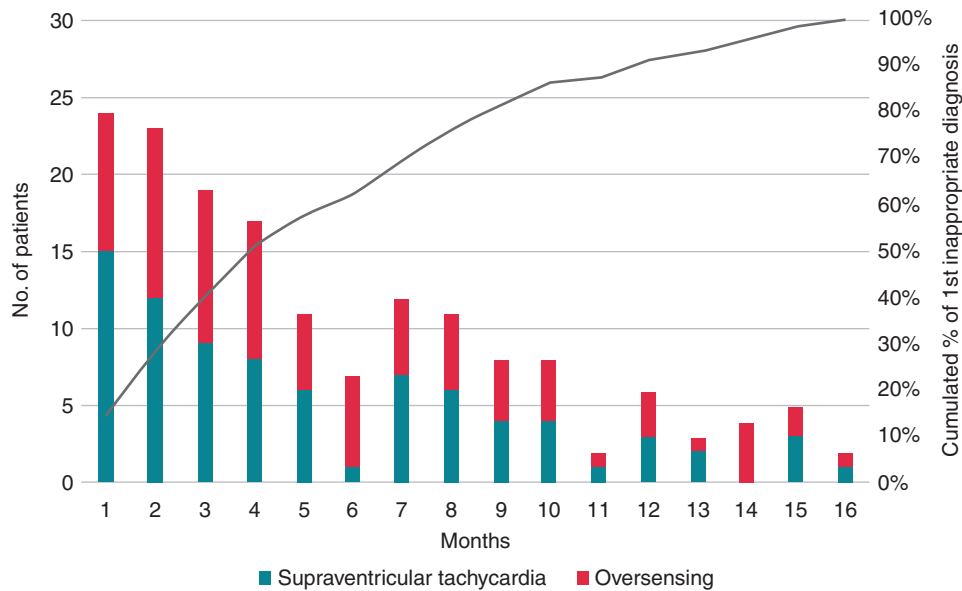


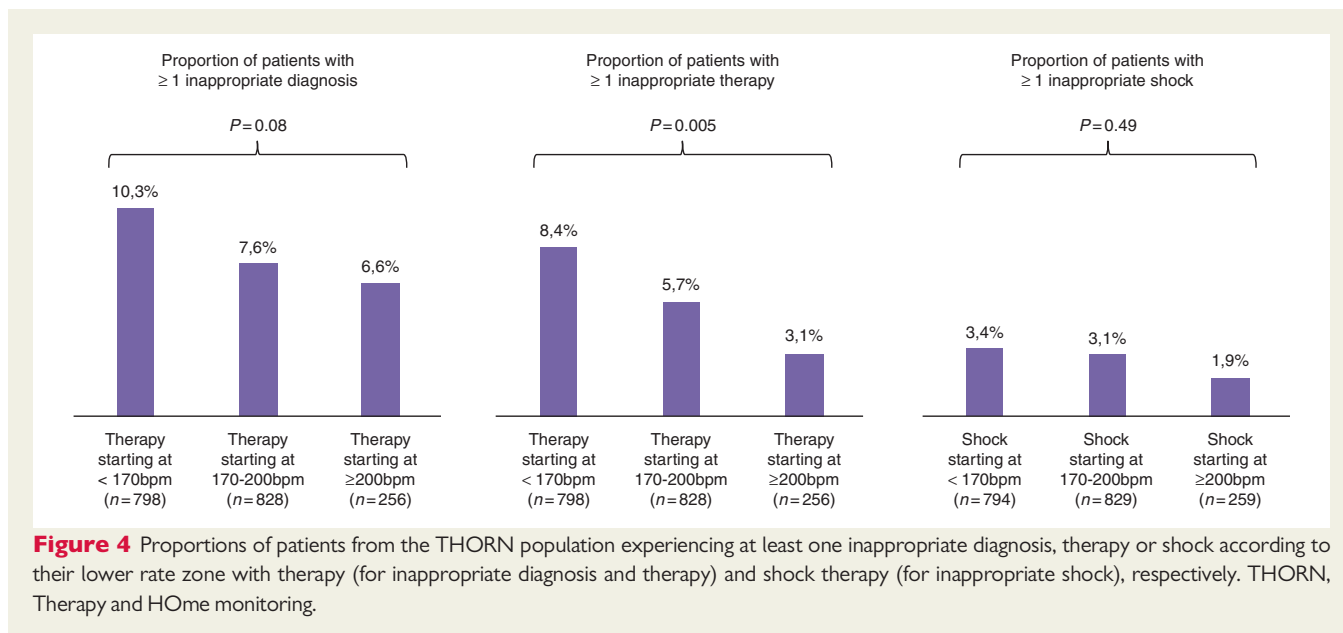
Figure 3 Cumulative occurrence and causes of the first inappropriate ICD diagnosis during follow-up (months) in the THORN population. ICD, implantable cardioverter-defibrillator; THORN, Therapy and HOme monitoring.

(26%) patients had at least one recurrence of an inappropriate diagnosis of the same cause, resulting in a therapy in six of them. Two out of the 15 patients (13%) with an inappropriate ICD shock had at least another inappropriate shock during the remaining FU. Among the recurrences of inappropriate diagnoses, 4/9 (44%) were due to SVT and 5/9 (56%) due to oversensing. Mean time between the inappropriate diagnosis management and the recurrence was 40 days (SD: 28 days). For the 25 (71%) others patients, the corrective action was efficient and there was no recurrence. One patient (welder) who refused the advices of his electrophysiologist was not included in the recurrence proportion.

Twenty-seven out of 504 (5%) patients died during FU, including 13 (3%) for cardiovascular reasons (nine for end-stage heart failure, two for asystole, one for ischaemic bowel disease, and one for stroke). No death case was directly related to an inappropriate diagnosis or therapy.

Discussion

Reduction of ICD therapies remains a main goal in ICD management, as appropriate, inappropriate, and unnecessary ICD shocks have



been associated with increased mortality⁴ and patient distress.¹⁴ Besides reducing the need for in-person evaluations by approximately 50%,¹² RM reduces significantly both appropriate as well as inappropriate ICD shocks by allowing early implementation of preventive actions.¹⁵

To the best of our knowledge, no previous study specifically reported the overall prevalence of inappropriate ventricular arrhythmia detection, including episodes without therapy, despite obvious relevance for early corrective actions. Our main results show that (i) inappropriate diagnoses occurred in 9% of patients implanted with an ICD at 13.7 months, with at least one inappropriate shock in more than one third of those patients; (ii) at least one other day with recording of an inappropriate diagnosis occurred in 30% of the DNPC periods, with an inappropriate therapy in 54% of them.

As expected, prevalence of inappropriate shocks (3%) as well as recurrence rate thereafter (13%) were both lower than previously reported without RM. In their study including patients implanted for primary and secondary prevention, Van Rees *et al.*¹⁶ describe a prevalence of inappropriate shocks of 7% at 1 year with a recurrence in 36% of patients. Importantly, despite the actual guidelines regarding ICD programming were not released by the time our patients were implanted, the slowest heart rate of the first VT zone with enabled therapy in our primary preventive subpopulation was 178 b.p.m. (SD: 21 b.p.m.), which is close to current recommendations.¹⁷ Supporting programming of higher detection frequencies for ventricular arrhythmia zones with therapy,⁸ we report higher rates of inappropriate therapies in case of lower detection frequencies. This most likely results from an increased rate of SVT misclassification, as supraventricular arrhythmias account for 50% of the inappropriate diagnoses in our population. Despite an average frequency of 173 b.p.m. (SD: 12 b.p.m.) to enter the first VT zone with therapy in the THORN population implanted for primary and secondary preventions, the occurrence of inappropriate shocks (3% at 13.7 months) remained in accordance with previous reports supporting programming of higher rate limits for VT and VF zones in primary prevention patients. In the

PREPARE study, incidence of inappropriate shocks in the experimental group was 4% after a FU of 1 year,⁷ and in the MADIT-RIT study, Moss *et al.*⁵ reported a first occurrence of inappropriate therapies and shocks of 5% and 3% in their delayed therapy cohort during 1.4 years of FU. Our low rate of inappropriate shocks, despite the slower rate limit for the first VT-zone with therapy, could be seen as a positive consequence of RM. Indeed, we expect RM to be especially useful in case of programming low detection frequencies and short detection duration. The notifications of inappropriate diagnoses in our population might have triggered therapeutic reaction by the physicians, possibly helping to avoid future inappropriate therapies and shocks. At the same time though, more than 30% of our inappropriate diagnoses were due to noise oversensing, which is difficult to avoid by device programming only.

Importantly, our data highlight that the majority of inappropriate VT and VF diagnoses occur during the first months after implantation. This emphasizes the need for tailoring the anti-tachycardia parameters to the patients' condition and for close monitoring during the first months after implantation with initiation of RM before hospital discharge. At the same time, 26% of our patients had at least a second inappropriate diagnosis of the same cause during the rest of their FU, indicating that inappropriate diagnoses are not a temporary issue.

Despite well-established guidelines,¹² our results demonstrate that use of RM can still be improved in real-life practice. Even if regular control of the web-based RM platform was advised and prompt corrective action by the medical team was expected, the median DNPC for inappropriate diagnoses remained 8 days (IQR 1.0–26.0) in the THORN population, with significant disparities depending on centres organization and inappropriate diagnosis origin. This might be seen as extremely long in comparison to the reaction time to clinical decision described in the CONNECT trial¹⁸ (median 4.6 days) or to the delay to patient contact reported in the IN-TIME study (median 1 day, IQR 0–6 days).¹⁰ That be, similarly to the time elapsed from event onset to physician evaluation in the TRUST trial¹⁹ (median 1 day, IQR 0–6 for VT and IQR 0–7 for VF notifications), we found a much shorter

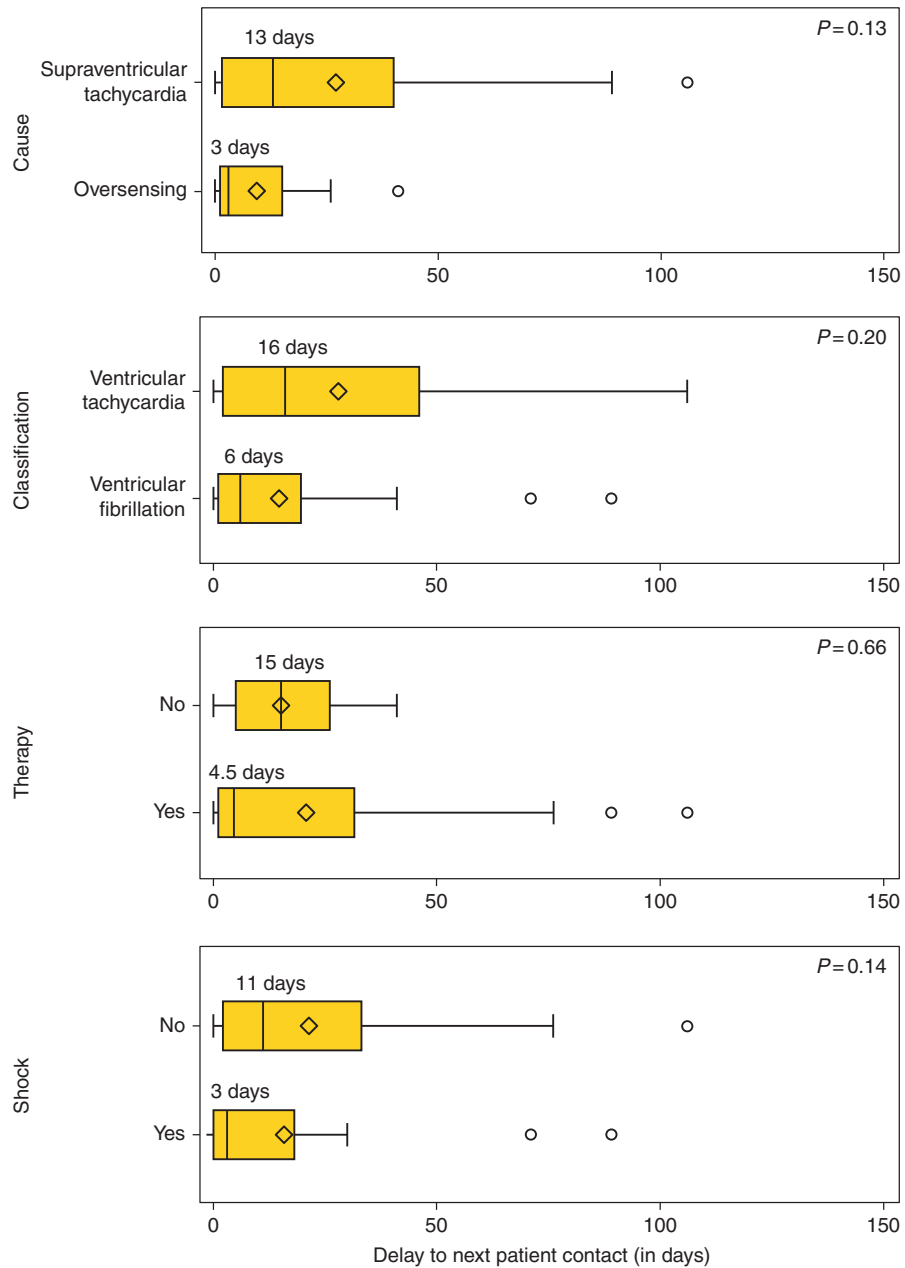


Figure 5 Median duration of the delay to next patient contact according to cause, classification of the event by the device, and delivery of an inadequate therapy.

time delay when considering only the delay between inappropriate diagnosis occurrence and confirmation of the episode on the RM platform (median of 1 day, IQR 0–3 days), reflecting the cause- and patient-based approach for patient contact in routine practice. In the IN-TIME study, the notifications were double-checked by the participating centres as well as the central monitoring unit and had to be followed by a standardized telephone call, which was obviously not the case in our prospective observational registry. Duration of the DNPC for all inappropriate diagnoses is nevertheless important, as we report intra-DNPC inappropriate diagnosis recurrences in 30% of available DNPC periods, with an inappropriate therapy in more

than half of them. Also, we found a correlation between the risk of intra-DNPC inappropriate diagnosis recurrence and the length of the DNPC. Reducing the DNPC should be addressed in a three steps process. First the patients should be educated and encouraged to transmit daily. Parthiban et al.²⁰ reported in their large meta-analysis a highly significant mortality benefit with the use of RM, which could be explained by the daily transmission. Second the implanting centres should define dedicated personal for daily controlling of their RM database. Last but not least, in case of a RM alert corrective actions should occur as soon as possible, which was obviously not the case in our real-life patients' population.

Table 2 Management of the first inappropriate diagnosis in the prospective subgroup

Management strategy	Patients (N = 35)
No patient contact due to incorrect interpretation of the inappropriate diagnosis episode	5 (14)
Watchful waiting strategy decided by the treating electrophysiologist without patient contact	2 (6)
Supplementary in-patient follow-up	20 (57)
Hospitalization	8 (23)
Corrective actions	
No specific action	16 (46)
Change in medication	8 (23)
Change in device programming	15 (43)
Ablation of supraventricular tachycardia	3 (9)
Lead revision	5 (14)

Data are reported as counts (%).

Limitations

Although our registry is the first large-scaled report concerning inappropriate diagnoses in ICD patients, we acknowledge some limitations. First, the evaluation of the prevalence of inappropriate diagnoses was retrospective for the THORN population. Despite most of the common cardiovascular characteristics are reported, not all data were available for each patient. To increase transparency, the exact number of patients considered for calculations are indicated in Table 1. Second, the programming of the ICD and the control of the RM platform was left to the discretion of individual physicians/centres. Important to mention, despite the number of intervals to fulfil tachycardia detection is not known, the lower therapy zone with therapy was close to current recommendations.¹⁷ Similarly, the kind of programming changes made during FU was not recorded. Third, one cannot exclude that some inappropriate episodes may have occurred while the patients were still hospitalized and had no RM set-up yet. However, RM was activated and functional from hospital discharge for all patients. Fourth, no comparison was done with occurrence of inappropriate diagnoses, therapies, or shocks in patients without RM, as the benefit of RM for inappropriate shock reduction has already been demonstrated.⁹ In that view, we aimed to focus on the occurrence of inappropriate diagnoses which could allow early corrective actions. Finally, our observations apply only to the Home Monitoring[®] system, as all patients of the THORN population were implanted with Biotronik ICD devices. Though we do not expect relevant differences in terms of ventricular arrhythmias transmission between the RM systems from the different ICD manufacturers, the transmission of complementary notifications, which varies much more between the different ICD companies, might additionally change the treatment strategies and the prognosis of the patients.

Conclusions

Inappropriate ICD diagnoses occurred in 9% of patients implanted with an ICD during the first 14 months. However, the rate of inappropriate shocks remained low in patients followed by RM, most probably due to early corrective actions. The delay to next patient

contact after inadequate ventricular arrhythmia diagnoses remains long in daily practice and should be optimized.

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References

1. Antiarrhythmics versus Implantable Defibrillators Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. *N Engl J Med* 1997;**337**:1576–83.
2. Kadish A, Dyer A, Daubert JP, Quigg R, Estes NA, Anderson KP et al. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. *N Engl J Med* 2004;**350**:2151–8.
3. Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med* 2002;**346**:877–83.

4. Proietti R, Labos C, Davis M, Thanassoulis G, Santangeli P, Russo V *et al.* A systematic review and meta-analysis of the association between implantable cardioverter-defibrillator shocks and long-term mortality. *Can J Cardiol* 2015;**31**: 270–7.
5. Moss AJ, Schuger C, Beck CA, Brown MW, Cannom DS, Daubert JP *et al.* Reduction in inappropriate therapy and mortality through ICD programming. *N Engl J Med* 2012;**367**:2275–83.
6. Gasparini M, Proclemer A, Klersy C, Kloppe A, Lunati M, Ferrer JB *et al.* Effect of long-detection interval vs standard-detection interval for implantable cardioverter-defibrillators on antitachycardia pacing and shock delivery: the ADVANCE III randomized clinical trial. *JAMA* 2013;**309**:1903–11.
7. Wilkoff BL, Williamson BD, Stern RS, Moore SL, Lu F, Lee SW *et al.* Strategic programming of detection and therapy parameters in implantable cardioverter-defibrillators reduces shocks in primary prevention patients: results from the PREPARE (Primary Prevention Parameters Evaluation) study. *J Am Coll Cardiol* 2008;**52**:541–50.
8. Clementy N, Challal F, Marijon E, Boveda S, Defaye P, Leclercq C *et al.* Very high rate programming in primary prevention patients with reduced ejection fraction implanted with a defibrillator: results from a large multicenter controlled study. *Heart Rhythm* 2017;**14**:211–7.
9. Guedon-Moreau L, Kouakam C, Klug D, Marquie C, Brigadeau F, Boule S *et al.* Decreased delivery of inappropriate shocks achieved by remote monitoring of ICD: a substudy of the ECOST trial. *J Cardiovasc Electrophysiol* 2014;**25**:763–70.
10. Hindricks G, Taborsky M, Glikson M, Heinrich U, Schumacher B, Katz A *et al.* Implant-based multiparameter telemonitoring of patients with heart failure (IN-TIME): a randomised controlled trial. *Lancet* 2014;**384**:583–90.
11. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA 3rd, Freedman RA, Gettes LS *et al.* ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices) developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2008;**51**:e1–62.
12. Slotwiner D, Varma N, Akar JG, Annas G, Beardsall M, Fogel RI *et al.* HRS Expert Consensus Statement on remote interrogation and monitoring for cardiovascular implantable electronic devices. *Heart Rhythm* 2015;**12**:e69–100.
13. STROBE Checklist for Cross-Sectional Studies 2007. <http://www.strobe-statement.org/index.php?id5available-che> (5 July 2015, date last accessed).
14. Pedersen SS, van Domburg RT, Theuns DA, Jordaens L, Erdman RA. Concerns about the implantable cardioverter defibrillator: a determinant of anxiety and depressive symptoms independent of experienced shocks. *Am Heart J* 2005;**149**: 664–9.
15. Guedon-Moreau L, Lacroix D, Sadoul N, Clementy J, Kouakam C, Hermida JS *et al.* A randomized study of remote follow-up of implantable cardioverter defibrillators: safety and efficacy report of the ECOST trial. *Eur Heart J* 2013;**34**:605–14.
16. Van Rees JB, Borleffs CJ, de Bie MK, Stijnen T, van Erven L, Bax JJ *et al.* Inappropriate implantable cardioverter-defibrillator shocks: incidence, predictors, and impact on mortality. *J Am Coll Cardiol* 2011;**57**:556–62.
17. Wilkoff BL, Fauchier L, Stiles MK, Morillo CA, Al-Khatib SM, Almendral J *et al.* 2015 HRS/EHRA/APHS/SOLAECE expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. *Europace* 2016;**18**: 159–83.
18. Crossley GH, Boyle A, Vitense H, Chang Y, Mead RH, Investigators C. The CONNECT (Clinical Evaluation of Remote Notification to Reduce Time to Clinical Decision) trial: the value of wireless remote monitoring with automatic clinician alerts. *J Am Coll Cardiol* 2011;**57**:1181–9.
19. Varma N, Epstein AE, Irimpen A, Schweikert R, Love C, Investigators T. Efficacy and safety of automatic remote monitoring for implantable cardioverter-defibrillator follow-up: the Lumos-T Safely Reduces Routine Office Device Follow-up (TRUST) trial. *Circulation* 2010;**122**:325–32.
20. Parthiban N, Esterman A, Mahajan R, Twomey DJ, Pathak RK, Lau DH *et al.* Remote monitoring of implantable cardioverter-defibrillators: a systematic review and meta-analysis of clinical outcomes. *J Am Coll Cardiol* 2015;**65**: 2591–600.