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RESEARCH LETTER

Low rates of inappropriate shocks in contemporary real-world implantable cardioverter defibrillator patients: the CARAT observational study

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Introduction

Implantable cardioverter defibrillator (ICD) implantation remains the mainstay of sudden cardiac death (SCD) prevention in high-risk patients. Among other complications of ICD therapy, inappropriate shocks negatively impact quality of life and may be associated with myocardial injury.[1] In the context of the recent development of non-transvenous ICD therapies, current real-world data may help decision-making in this vulnerable patient cohort.

Methods

Study design

The Clinical and Device Functional Assessment of Real World ICD Patients (CARAT) trial is a prospective, multi-centre, international, observational, post-market study of all approved and commercialized CE and/or Food and Drug Administration ICD devices [VR/DR/cardiac resynchronisation therapy defibrillator (CRT-D)] from MicroPort CRM® (Clamart, France), registered at ClinicalTrials.gov (NCT02341768). The subjects provided informed consent during the index hospital stay of implantation in accordance with ISO 14155 and local regulations and were then followed-up over 2 years; a centralized and independent review of all ICD therapies were performed to adjudicate appropriateness.

Statistical analysis

Mean and standard deviation were calculated for continuous variables. For time-to-event variables, the Kaplan–Meier cumulative incidence with death as a competing risk method was used. The estimates were provided with time points every 2 months. Subjects who had prematurely discontinued without any event were censored at the date of discontinuation.

Table 1 Baseline data

Population characteristics ($n = 2028$)	
Age	67 years (IQR: 59–75)
Females	21.1%
Primary prevention of SCD	77.0%
LVEF	30% (IQR: 25–35)
Ischaemic/idiopathic dilated/other CMP	51%/29%/20%
NYHA class I/II/III/IV	15.9%/51.7%/31.0%/1.4%
Advanced renal failure/diabetes	15%/25.4%
Chronic respiratory disease	12.5%
History of stroke	7.5%
HF hospitalization during last 6 months	15.8%
Paroxysmal/persistent/permanent AF	11.4%/5%/9.2%
Atrial flutter and/or atrial tachycardia	3.5%
AVB I/II/III	7.2%/1.2%/2.2%
SND	3.5%
LBBB/RBBB/IVCD	23.5%/6.2%/2.0%
Previous VT/SVT ablation	3%/1.4%

IQR, interquartile range; SCD, sudden cardiac death; VT, ventricular tachycardia; LBBB, left bundle branch abnormality; AF, atrial fibrillation; LVEF, left ventricular ejection fraction; CMP, cardiomyopathy; AVB, atrioventricular block; SND, sinus node disease; RBBB, right bundle branch block; IVCD, intraventricular conduction delay; SVT, supraventricular tachycardia; HF, heart failure; NYHA, New York Heart Association.

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Results

Patient characteristics

From 1 July 2015, to 31 October 2017, a total of 2032 patients, either as a *de novo* implantation ($n = 1463$, 72.1%) or replacement ($n = 565$, 27.9%), were enrolled at 94 sites from 12 countries in Europe and North-America. As four patients were not implanted, 2028 patients (1601 males, 427 females) were analysed. Baseline characteristics are given in *Table 1*. Final follow-up visit after 24 months was available in 73.8% ($n = 1496$) study participants. Apart from death (9.4%, $n = 169$), reasons for premature study discontinuation were lost to follow-up in 5.0% ($n = 102$), withdrawal by the patient in 2.8% ($n = 57$), completion of the study without final visit in 2.2% ($n = 45$), non-fatal adverse events in 1.0% ($n = 20$), and other reasons in 6.7% ($n = 136$).

Tachyarrhythmia detection and therapy programming

Detection programming was very similar across CRT-D, dual chamber, and single chamber ICD models. A slow ventricular tachycardia (VT) zone was enabled in more than 50% of study participants from as low as 150 beats per minute (bpm), with the vast majority being programmed as a monitoring zone without therapy. A VT zone was enabled from 170 bpm on average, with AntiTachycardia Pacing 1 (ATP1) burst/AntiTachycardia Pacing 2 (ATP2) ramp and shocks in the vast majority of patients. A fast VT zone favouring antitachycardia pacing (ATP) delivery was activated in more than 80% of patients allowing rhythm detection until 240 bpm. There were only few and non-meaningful differences in tachyarrhythmia detection programming across countries or between patients receiving ICD therapy because of primary or secondary prevention of SCD. A so-called 'shock box' programming (without any ATP therapy, ventricular fibrillation (VF) zone between 198 and 206 bpm) was programmed in only 37 study participants (1.8%), mainly in patients with the ICD implanted for primary prevention of SCD.

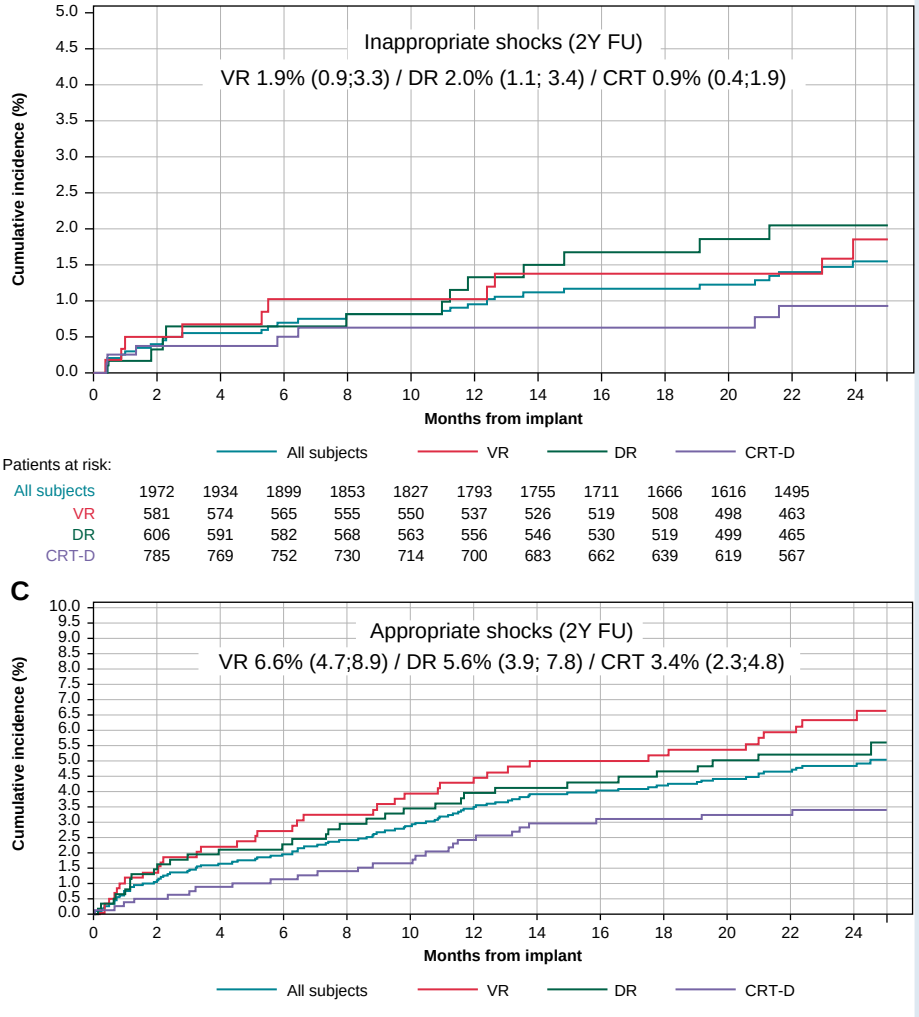
Appropriate and inappropriate ICD therapies

Within 2 years, 13.4% ($n = 250$) and 3.8% ($n = 69$) received appropriate and inappropriate ICD therapies, respectively. Appropriate and

A

Enrollment per country	
France	36.3%
Spain	15.5%
Italy	11.3%
Germany	8.5%
Portugal	8.4%
United Kingdom	5.0%
Canada	4.1%
Austria	3.7%
Netherlands	3.7%
Slovak Republic	1.5%
Czech Republic	1.4%
Switzerland	0.3%
ICD models	
VR	600
DR	624
CRT	804
All	2028
SCD Prevention	
Primary	77%
Secondary	23%

B



C

Figure 1 (*A*) Enrolment per country, ICD model, and type of SCD prevention. (*B*) Cumulative incidence of inappropriate shocks per type of ICD model. (*C*) Cumulative incidence of appropriate shocks per type of ICD model. ICD, implantable cardioverter defibrillator; SCD, sudden cardiac death.

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inappropriate ICD shocks occurred in 5.0% ($n = 95$) and 1.6% ($n = 29$) of patients, respectively, as depicted in *Figure 1*.

Discussion

The large prospective international dataset of the CARAT study reports a remarkably low rate of inappropriate shocks in real-world contemporary ICD therapy (1.6% within 2 years). This rate slightly varies across ICD models; however, the confidence intervals overlap. Avoiding inappropriate shocks is a key component of quality of life and of ICD acceptance by patients.[2]

As the PARAD+® algorithm had been used as default tachyarrhythmia detection algorithm in the presence of a functional atrial lead, CARAT confirms results of previous studies such as OPTION[3,4] or ISIS-ICD[5] in terms of arrhythmia discrimination in dual-chamber devices. The present study also reports low inappropriate shocks in single-chamber devices, where arrhythmia discrimination is based on a combination of stability, acceleration, and 'long cycle gap' to identify atrial fibrillation.

In the PRAETORIAN trial with a median follow up of 49.1 months, rates of inappropriate ICD shocks were remarkably higher, both in patients implanted with a subcutaneous ICD (9.7%) and with a transvenous ICD (7.3%).[6,7] The PIVOTAL trial testing the new extravascular ICD approach reported that even 9.7% of patients implanted with a substernal ICD lead received inappropriate shocks during a mean follow-up of 10.6 months.[8] In transvenous ICD trials, inappropriate shocks were more common in the EU-CERT trial (7% within 2.7 years),[9] the UMBRELLA study (5.0% at 2 years),[10] and—to a much lesser degree—in the PainFree SST sub-study (2.8% in patients with a dual chamber ICD or CRT-D device and 3.7% in patients with a single chamber ICD within 2 years).[11] The rate of inappropriate shocks in the VR patients in the present study (1.9% at 2 years) also compares favourably with the annual rate of 6.4% reported in a systematic review.[12]

Appropriate ICD therapy was delivered in 13.4% of the study cohort, whereas appropriate shocks were mandated in 5.0% of patients at 2 years. Consistently with previous studies,[5] a lower rate of appropriate shocks is found in the CRT-D arm. The rate of appropriate ICD shocks in CARAT was lower than in recently published trials such as the EU-CERT trial (7.1% within 2.7 years)[9] and the PRAETORIAN trial (19.5% in the subcutaneous ICD subgroup and 13.5% in the transvenous ICD subgroup, median follow-up 49.1 months)[6,7] and comparable to the DANISH trial (11.5% within 5.5 years),[13] potentially associated with a reduced proportion of ischaemic heart failure aetiology in the present study (51%).

The CARAT study further offers the opportunity to confirm the adoption of recommendations for ICD programming in clinical routine, according to the expert consensus on optimal ICD programming and testing.[14,15] Prolonged detection settings for tachyarrhythmias with duration criteria of at least 6–12 s or 30 intervals were on average programmed shorter in CARAT patients, namely 20–24 cycles in the VT and 10 cycles in the VF zone, respectively; therefore, discrimination performance was obtained without compromise on the time to therapy delivery. Detection zones and therapy programming were globally well aligned with consensus, allowing to fully benefit from ICD tachyarrhythmia detection and therapy capabilities.

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Conflict of interest: Y.P. is an employee of Microport CRM® (Clamart, France). All other authors do not report any conflict of interest.

Data availability

All data are available on a reasonable request to the sponsor of the trial.

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