Very high rate programming in primary prevention patients with reduced ejection fraction implanted with a defibrillator: Results from a large multicenter controlled study

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BACKGROUND Programming implantable cardioverter-defibrillators (ICDs) with a high-rate therapy strategy has proven to be effective in reducing shocks and is associated with a reduced mortality.

OBJECTIVE We sought to determine the impact of a very high rate cutoff programming strategy on outcomes in patients with a primary indication for an ICD due to reduced left ventricular ejection fraction.

METHODS Using data from the multicenter French DAI-PP registry, this cohort-controlled study compared outcomes in 500 patients programmed with a very high rate cutoff (VH-RATE group: monitor zone 170–219 beats/min; ventricular fibrillation zone ≥220 beats/min with 13 ± 4 detection intervals) with 1500 matched control patients programmed with 1 or 2 therapy zone. All ICDs were implanted for primary prevention in patients with systolic dysfunction. Risks of events were compared after propensity score matching of sex, age, ejection fraction, New York Heart Association class, cardiomyopathy, atrial fibrillation, and type of device.

RESULTS After a mean follow-up of 3.6 ± 2.3 years, VH-RATE programming was associated with a reduction of appropriate therapy risk (hazard ratio [HR] 0.40; 95% confidence interval [CI] 0.31–0.51; $P < .0001$) and inappropriate shock (HR 0.42; 95% CI 0.27–0.63; $P < .0001$). It was also associated with a decreased risk of sudden cardiac death (HR 0.43; 95% CI 0.17–0.99; $P = .04$) as compared with patients programmed with 2 therapy zones. There was no significant difference in overall survival between the groups.

CONCLUSION In patients implanted with an ICD in primary prevention with left ventricular dysfunction, very high rate cutoff programming (single therapy zone ≥220 beats/min) was associated with a 60% reduction of appropriate therapies as well as inappropriate shocks, without affecting mortality.

KEYWORDS Implantable cardioverter-defibrillator; Primary prevention; Sudden cardiac death; High rate; Programming; Appropriate; Inappropriate; Antitachycardia pacing; Shock; Outcome

Introduction

Implantable cardioverter-defibrillators (ICDs) reduce all-cause mortality in primary prevention of sudden cardiac death in patients with cardiomyopathy and reduced left ventricular ejection fraction (LVEF).[1] These benefits are spoiled by a significant increase in morbidity through appropriate shocks in about 1 of 5 patients and inappropriate shocks in about 1 of 7 patients.[2] These internal electrical shocks have been shown to be associated with increased mortality[3] and are involved in premature battery depletion.

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Strategies to reduce the use of ICD therapies are recommended.[4] A strategy of programming longer detection intervals has proven to be safe and effective in reducing appropriate and inappropriate discharges.[5–8] High-rate cutoff programming is another promising strategy, also associated with reduced mortality in 1 study.[5] "Very high rate" programming, with a therapy onset rate of >220 beats/min, has also shown to be associated with low therapy rate.[9] We sought to assess the efficacy and safety of this very high rate strategy in a large, long-term follow-up and controlled study.

Methods

Population

The DAI-PP multicenter registry provides long-term data on 5576 patients implanted with an ICD in primary prevention in 12 high-volume centers in France. Our institutional ethics committee on human research approved the study protocol. All patients signed informed consent before inclusion. Patient information was then de-identified. The trial has been registered at www.clinicaltrials.gov under number NCT01992458.

Consecutive patients with ischemic or nonischemic cardiomyopathy and left ventricular systolic dysfunction who underwent the implantation of an ICD in primary prevention of sudden cardiac death between January 2005 and January 2012 were included. Exclusion criteria were as follows: age <18 years, a previous documented spontaneous sustained ventricular arrhythmic event, and previous implantation of an ICD.

Device programming

Patients were programmed according to the protocols of local centers and then divided into 3 groups according to the tachycardia settings (Table 1). Bradycardia settings were left to the physician's preference.

Table 1 ICD programming at baseline in the VH-RATE group and the DAI-PP subgroups

Variable	VH-RATE group (n = 500)	1-Zone group (n = 300)	2-Zone group (n = 1200)
Monitoring	LR: 170 ± 0.6 beats/min	LR: 172 ± 10 beats/min	LR: 160 ± 9 beats/min
VT	—	—	LR: 177 ± 7 beats/min NID: 20 ± 6 ATP: 9 ± 3 Shocks: Yes Discrimination: On Timers: Off
VF	LR: 221 ± 1.0 beats/min NID: 13 ± 4	LR: 200 ± 0.2 beats/min NID: 16 ± 3	LR: 222 ± 7 beats/min NID: 16 ± 6

ATP = number of sequences of antitachycardia pacing (bursts or ramps); ICD = implantable cardioverter-defibrillator; LR = lower detection rate; NID = number of intervals to fulfill detection; VF = ventricular fibrillation zone; VT = ventricular tachycardia zone.

VH-RATE group

All patients from 1 center (CHU Tours, France) were programmed with a monitoring-only zone starting at a frequency of ≥170 beats/min and a high-rate ventricular fibrillation (VF) zone (no discrimination) at ≥220 beats/min.[9] Discrimination algorithms in the monitoring zone were set "on," unless unnecessary, such as in patients with complete atrioventricular block. Nominal settings for the number of detection intervals were programmed in both zones. Shock therapies in the VF zone were programmed to maximum output.

1-Zone group

Patients from 2 centers were programmed with a single therapy (VF) zone above 200 beats/min.

2-Zone group

Patients from 6 centers were programmed with a fast ventricular tachycardia (VT) zone (discriminators "on") at a frequency of 180 beats/min with antitachycardia pacing (ATP) and shocks as well as a VF zone above 220 beats/min.

Follow-up and outcomes

Patients were monitored once or twice a year at the implantation center. Clinical evaluation and device testing were carried out at each follow-up visit. At each implantation center, the treated events were reviewed and interpreted by a local committee and classified as appropriate (ventricular arrhythmias) or inappropriate (supraventricular arrhythmias or oversensing). Untreated ventricular events occurring in the monitoring zone in the VH-RATE group were collected. Causes of death were also classified as sudden cardiac death, other cardiac death, and noncardiac death.

Time to first ICD therapy, to first appropriate therapy (ATP or shock), to first inappropriate shock, and to death were recorded, as well as the cause of death. Follow-up ended with death, heart transplantation, or definitive ICD removal.

Statistical analyses

All statistical analyses were performed using JMP version 9.0 (SAS Institute Inc., Cary, NC) and SPSS version 22.0 (IBM Corporation, Armonk, NY).

Descriptive statistics were reported as mean ± SD for normally distributed continuous variables. Median and interquartile range were also reported, when relevant. All comparisons between groups were performed using parametric tests.

The 1-Zone and 2-Zone groups were matched with the VH-RATE group using propensity score calculation; the propensity score model included the relevant covariates that might affect outcomes: age, sex, LVEF, type of cardiomyopathy (ischemic or nonischemic), New York Heart Association class, history of atrial fibrillation, and type of device (single-chamber, dual-chamber, or biventricular). Patients with a propensity score of <0.1 were systematically excluded. Nearest-neighbor matching was performed in the remaining patients.