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A Comparison of Empiric to Physician-Tailored Programming of Implantable Cardioverter-Defibrillators

Results From the Prospective Randomized Multicenter EMPIRIC Trial

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OBJECTIVES The purpose of this randomized study was to determine whether a strategically chosen standardized set of programmable settings is at least as effective as physician-tailored choices, as measured by the shock-related morbidity of implantable cardioverter-defibrillator (ICD) therapy.

BACKGROUND Programming of ventricular tachyarrhythmia (ventricular tachycardia [VT] or ventricular fibrillation [VF]) detection and therapy for ICDs is complex, requires many choices by highly trained physicians, and directly influences the frequency of shocks and patient morbidity.

METHODS A total of 900 ICD patients were randomly assigned to standardized (EMPIRIC, n = 445) or physician-tailored (TAILORED, n = 455) VT/VF programming and followed for 1 year.

RESULTS The primary end point was met: the adjusted percentages of both VT/VF (22.3% vs. 28.7%) and supraventricular tachycardia or other non-VT/VF event episodes (11.9% vs. 26.1%) that resulted in a shock were non-inferior and lower in the EMPIRIC arm compared to the TAILORED arm. The time to first all-cause shock was non-inferior in the EMPIRIC arm (hazard ratio = 0.95, 90% confidence interval 0.74 to 1.23, non-inferiority $p = 0.0016$). The EMPIRIC trial had a significant reduction of patients with 5 or more shocks for all-cause (3.8% vs. 7.0%, $p = 0.039$) and true VT/VF (0.9% vs. 3.3%, $p = 0.018$). There were no significant differences in total mortality, syncope, emergency room visits, or unscheduled outpatient visits. Unscheduled hospitalizations occurred significantly less often ($p = 0.001$) in the EMPIRIC arm.

CONCLUSIONS Standardized empiric ICD programming for VT/VF settings is at least as effective as patient-specific, physician-tailored programming, as measured by many clinical outcomes. Simplified and pre-specified ICD programming is possible without an increase in shock-related morbidity. (J Am Coll Cardiol 2006;48:330–9) © 2006 by the American College of Cardiology Foundation

The Center for Medicaid and Medicare Services recently published expanded coverage for implantable cardioverter-defibrillator (ICD) therapy based on the mortality benefit demonstrated in the SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial), DEFINITE (Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation) trial, the MADIT-II (Multicenter Automatic Defibrillator Implantation Trial-II), and the COMPANION (Comparison of Medical Therapy, Resynchronization, and Defibrillation Therapies in Heart Failure) trial (1–5). However, ICDs can be associated with patient morbidity and worse quality of life when the patient receives painful shocks, especially multiple shocks (6–9). With expanded indications for ICD implantation, concern has developed about who should implant, program, and follow these devices and what kind of training is required for these individuals (10–13). More importantly, how can consistent expert care be delivered to every patient in order for them to receive the benefits of ICDs without substantial morbidity?

Implantable cardioverter-defibrillator therapy can involve many complex choices, including more than 100 programmable parameter values that determine the detection and treatment of rhythms presented to the device. There are multiple programming strategies for reducing the number of morbid events related to shocks. Some publications have suggested that antitachycardia pacing (ATP) is not needed for patients without a prior history of a clinical tachycardia (2,10), whereas others have suggested that more than 70% of ventricular tachyarrhythmias can be terminated safely without a shock if ATP is given a chance (7,14,15). It has been assumed that patient-specific customization of all these parameters is crucial to the ICD's appropriate response, so that all life-threatening arrhythmias are treated with minimal shocks delivered to the patient for non–life-threatening arrhythmias. This assumption is based on two premises: 1) the physician programming the ICD knows which strategies will produce the best results, and 2) a patient-specific customization of the programming will produce the best protection with the least morbidity.

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Abbreviations and Acronyms

AF	= atrial fibrillation
AFL	= atrial flutter
AT	= atrial tachycardia
ATP	= antitachycardia pacing
CI	= confidence interval
EMPIRIC	= Comparison of Empiric to Physician-Tailored Programming of Implantable Cardioverter-Defibrillators trial
GEE	= general estimating equation
HR	= hazard ratio
ICD	= implantable cardioverter-defibrillator
RR	= relative risk
SVT	= supraventricular tachycardia or other non-VT/VF event
VF	= ventricular fibrillation
VT	= ventricular tachycardia

This investigation tests the hypothesis that, as measured by shock-related morbidity, an initial programming strategy using a well-constructed set of tachyarrhythmia detection and therapy parameters (EMPIRIC parameters), when consistently applied to a large group of unselected ICD patients, would be as successful as an individualized patient-specific, physician-tailored (TAILORED) set of parameters. The hypothesis requires that the EMPIRIC parameters perform as well as the control group in two ways: 1) percentage of ventricular arrhythmias that are shocked, and 2) percentage of supraventricular tachycardia or other non-ventricular tachycardia (VT)/ventricular fibrillation (VF) events (SVTs) that are shocked.

METHODS

The EMPIRIC (Comparison of Empiric to Physician-Tailored Programming of Implantable Cardioverter-Defibrillators) trial was a worldwide, multicenter, single-blind, non-inferiority, parallel-group, 1:1 randomized trial of ICD programming (16). Enrollment was conducted at 54 centers in the U.S., Canada, Europe, and the Middle East between August 2002 and October 2003. The institutional review board at each center approved the study protocol, and written informed consent was obtained from each patient.

PARTICIPANTS AND ICD PLACEMENT

All patients had standard indications for ICD placement as defined by the American College of Cardiology/American Heart Association/North American Society for Pacing and Electrophysiology guidelines (17). Patients were considered to have a secondary prevention indication for ICD placement if there was a history of spontaneous sustained VT/VF or syncope with suspected VT. All other patients were considered to have a primary prevention indication. Patients had to be undergoing their first placement of an ICD and be free of permanent atrial fibrillation (AF).

All patients received a Model 7274 Marquis DR ICD (Medtronic Inc., Minneapolis, Minnesota) and were randomized after successful implantation testing of the atrial and ventricular leads for sensing, capture, VF detection, and defibrillation with a 10-J safety margin.

RANDOMIZATION

Patients were randomized to have the tachyarrhythmia detection and therapy programmed to prescribed values (EMPIRIC) or to values determined by the treating physician (TAILORED). The patients were blinded to the randomization.

Randomization was done at the data-coordinating center and was stratified by the treatment center. The randomization was based on permuted blocks with a block size of 2 initially, followed by a block size of 2 or 4 with a probability of 0.5 each. Since the incidence and prevalence of spontaneous VT/VF and SVT may be different between primary prevention patients, randomization was also stratified by ICD indication (secondary vs. primary).

PROGRAMMING

Tachyarrhythmia detection and therapy settings were strategically chosen in the EMPIRIC arm to reduce shocks for VT/VF and SVTs and to avoid untreated slow VT (Table 1). The key strategies included: 1) avoid detecting non-sustained tachycardias;, 2) avoid detecting SVTs as VT; 3) empirical ATP for slow and fast VTs; and 4) high-output first shocks. A more detailed discussion of these strategies is found in a paper outlining the rationale for the study design (16). The VT/VF programming was set at the discretion of the implanting electrophysiologist in the TAILORED arm. All implanters and centers invited to participate had long-established ICD placement and programming practices. In order to provide similar data collection in both arms, the VT zone was programmed to monitor rhythms faster than 150 beats/min in the TAILORED arm if the investigator chose to have VT therapies off. Bradycardia settings were programmed at the discretion of the investigators in both arms.

Table 1. EMPIRIC Arm Programming of VT/VF Settings

Detection	Threshold	Detect Beats	Therapies
VF on	250 beats/min	18 of 24	30 J × 6
FVT via VF	200 beats/min	(18 of 24)	Burst (1 sequence), 30 J × 5
VT on	150 beats/min	16	Burst (2), ramp (1), 20 J, 30 J × 3

Supraventricular tachycardia criteria on: atrial fibrillation/atrial flutter, sinus tach (1:1 VT-ST boundary = 66%), SVT limit = 200 beats/min. Burst ATP: 8 intervals, R-S1 = 88%, 20 ms decrement. Ramp ATP: 8 intervals, R-S1 = 81%, 10 ms decrement.
ATP = antitachycardia pacing; FVT = fast ventricular tachycardia; VF = ventricular fibrillation; VT = ventricular tachycardia.