Not too late, not too fast!!

C. Leclercq*, C. Daubert, and P. Mabo

CHU Rennes, Service de Cardiologie et Maladies Vasculaires, INSERM U 642, CIC-IT 0804, 35000 Rennes, France

Online publish-ahead-of-print 27 October 2009

This editorial refers to ‘A simplified biventricular defibrillator with fixed long detection intervals reduces implantable cardioverter defibrillator (ICD) interventions and heart failure hospitalizations in patients with non-ischaemic cardiomyopathy implanted for primary prevention: the RELEVANT [Role of long dEtection window programming in patients with LEft VentriculAr dysfunction, Non-ischemic eTiology in primary prevention treated with a biventricular ICD] study’1, by M. Gasparini et al., on page 2758

Intracardiac cardioverter defibrillators (ICDs) are expected to detect and to treat ventricular arrhythmias (VAs) in patients with previously documented VAs (secondary indication) or in patients at high risk of occurrence of VAs (primary indication).1,2 The treatment process includes the detection of VAs followed by the delivery of a therapy, i.e. antitachycardia pacing (ATP) and/or shocks. One of the main challenge of the devices is to detect the arrhythmia correctly, including noise rejection, and to identify its origin, i.e. supraventricular or ventricular, and thus to deliver therapy or not. The technical objective is to deliver only appropriate therapy and to avoid inappropriate therapies especially shocks (high specificity), but without the risk of underdetection of a life-threatening arrhythmia (high sensitivity).1,2 The detection and classification of VAs are essentially based on two additional parameters: the ventricular rate and the number of intervals reaching this threshold needed to be detected [number of intervals to be detected (NID)]. As a mandatory first step, these two parameters are fundamental for arrhythmia detection. Additional parameters, only available in the ventricular tachycardia (VT) zone, such as the sudden onset of the episode, the relationship of the atrial and ventricular activities (only in dual-chamber devices), or the intracardiac electrocardiogram (iEGM) morphology may be used for a better arrhythmia classification. Until now any device has not considered the haemodynamic tolerance of VAs to whether on not therapy has been delivered. The optimization of the programming of the delivery of antitachycardia therapy of an ICD is challenging, with the need to treat life-threatening VAs, VT and ventricular fibrillation (VF) urgently and efficiently and the avoidance of inappropriate therapies, especially shocks. Another challenge is not to treat too quickly in order to avoid unnecessary therapies particularly in self-terminating arrhythmias which are relatively frequent, but also not too late in order to prevent syncope. In clinical practice the programming of an ICD is still empirical and individually selected, and the need for objective data to improve device programming is an important issue.

Gasparini et al. have reported an interesting study designed to compare two strategies of detection (based on the NID) and treatment of VAs in patients with non-ischaemic cardiomyopathy with indication for an ICD for primary prevention and candidates for cardiac resynchronization therapy (CRT).3 (i) one conventional strategy with a standard CRT-D ‘full-featured device’ with a ‘standard’ 12/16 NID, i.e. the control group; and (ii) the ‘Protect’ strategy with a full-featured CRT pacing device combined with simplified, ‘easy to use’ ICD features with a fixed, long detection interval (30/40 NID) with one fixed 88% ATP burst in the fast VT window and full shock capability.

The potential advantage of the latter programming is to alter the delivery of antitachycardia therapy and thus to avoid treatment of self-terminating VAs, and also of supraventricular arrhythmias (Figure 1).

In this prospective, controlled, parallel but non-randomized study, from 2004 to 2007, 164 patients were included in the ‘Protect’ group and 160 in the control group, and were followed-up for a mean period of 14 months.

In the Protect group, 91% of ventricular tachyarrhythmia episodes (282/311) terminated spontaneously within the 13–29 detection interval; most of these arrhythmias would have been treated in the control group with an NID of 12/16. The analysis of these self-terminating VAs showed that 66% of VF and 91% of fast VT self-terminated within 29 beats, and 92% of VT episodes within 31 beats.

The number of inappropriately detected episodes due to atrial arrhythmias, T wave oversensing, or noise was significantly lower in the Protect group than in the control group (20 vs. 242; P<0.01). In both group, 90% of these inappropriately detected episodes were due to supraventricular tachycardias.

VA episodes which were appropriately treated as VAs were significantly lower in the Protect group (26 episodes in nine patients) than in the control group (241 episodes in 26 patients). Inappropriately treated episodes were also dramatically reduced in the...
Protect group, with only 10 events as compared with the control group with 48 events ($P<0.0001$).

More importantly, the total number of delivered shocks was significantly decreased in the ‘Protect’ group, 22 vs. 59 ($P<0.001$). This dramatic reduction was mainly due to the decrease of inappropriate shocks, five in the protect group vs. 30 in the control group ($P<0.0001$), whereas the reduction of appropriate shocks in the Protect group was not statistically significant 17 vs. 29 ($P<0.057$), but an interesting trend was observed.

Another important finding was that only two episodes of syncope in the Protect group were reported: one was due to a prolonged detection of a fast VT and the other was due to a fast VT acceleration after ATP. In the control group, three episodes of syncope were observed, all after a VT acceleration after ATP.

This study was conducted in a selected population with CRT and primary ICD indications with non-ischaemic cardiomyopathy, probably the ‘ideal’ population, as the number of non-sustained arrhythmias is high in these patients. Previous reports showed that the incidence of self-terminating ventricular tachyarrhythmias was greater in patients with non-ischaemic cardiomyopathy, regardless of indication.$^4$

The rate of VAs and ICD therapies in the CRT population was evaluated by Ypemburg et al. in 120 patients implanted with a biventricular ICD and primary ICD indications: VT and VF were observed in 24% of the patients with a rate of 21% of appropriate ICD therapies and a rate of 5% of inappropriate shocks mostly due to atrial arrhythmias.$^5$

Unfortunately, details of the programming of the device (arrhythmia detection and treatment) was not provided in this study. Fifty-two per cent of the patients had a non-ischaemic cardiomyopathy and the aetiology of the cardiomyopathy was not found to be a predictive factor of appropriate ICD therapy, confirming the data from the Ventak CHF, Contak CD, and InSync studies.$^6,7$ A retrospective analysis of the MIRACLE ICD trial, including 415 patients (44% with non-ischaemic cardiomyopathy) with primary prevention showed that 14% of the population receiving CRT had at least one appropriately detected episode.$^8$ Among the population who had an appropriate or inappropriate episode, 68% of the patients had only appropriate episodes, 21% had only inappropriate episodes, and 11% experienced both, the inappropriate episodes being mainly due to sinus tachycardia. The same proportion of appropriate and inappropriate shocks was observed in the companion trial.$^9$ Another important finding in the MIRACLE ICD study was that in reviewing device-classified VF episodes spontaneously terminated during capacitor charging of typically 8–12 s, 48% of the VF episodes terminated before delivery therapy, the percentage being similar to those observed in the pain-free Rx II trial using a 12/24 NID and thus an additional detection delay of 3 s during capacitor charging.$^{10,11}$

The potential advantages of a program with a longer NID in the fast VT/VF zones have already been evaluated in patients with left ventricular dysfunction and ICD indications in the EMPIRIC and PREPARE trials, but in a different population from that in the RELEVANT study.$^{2,12,13}$ In the EMPIRIC trial, most of the patients have a secondary prevention ICD indication and an ischaemic cardiomyopathy, and all patients received a dual-chamber ICD.$^{12}$ In the PREPARE trial, including 700 patients with a primary prevention ICD indication, only 35% were implanted with a biventricular ICD and most of them had an ischaemic cardiomyopathy.$^{13}$ The EMPIRIC study, using a shorter NID than those tested in the RELEVANT study, showed that an empiric programming with an NID of 18/24 was at least as effective as patient-specific, physician-tailored programming without an increase in shock-related morbidity.$^{1,2}$ The PREPARE trial, using an NID of 30/40 with patients from the EMPIRIC and MIRACLE-ICD trials as the control cohort, showed that a long NID significantly decreased the risk of appropriate and inappropriate shocks without increasing the occurrence of untreated VT and arrhythmic syncope.$^{1,2,13}$

Previous studies have shown that most inappropriate therapies are determined by high ventricular rate atrial tachyarrhythmias (ATs) and we can hypothesize that a longer NID would be favourable for two reasons: the spontaneous termination of ATs and, more importantly, especially for patients with persistent or permanent atrial fibrillation, the variations of the ventricular rhythm leading to only transient crossing above the threshold value for VT/VF detection.$^{1,8,10,12,13}$ In fact in the RELEVANT population, the proportion of patients with permanent atrial fibrillation was high, 17.7% in the Protect group and 14.4% in the control group ($P=NS$), but was consistent with data from previous surveys.$^{14,15}$ However, it would be too simplistic to hope that a prolonged NID would avoid all the inappropriate therapies and especially shocks with their major impact on the quality of life of the patients.$^{1,2}$ Indeed inappropriate shocks may also be due to oversensing (T wave, electrical interference, etc.) or lead fractures which remain a major problem in the ICD population.$^{16}$

The RELEVANT study has some limitations as stated honestly by the authors themselves. The main limitation was the lack of randomization which restricts the power of this study. Furthermore, we do not know how the patients were selected in both groups; during the same period or during two different periods during the inclusion time. However, in the Protect group, an interesting evaluation of the detected VA using the 12/16 NID was provided, showing that the number of appropriately detected episodes was similar to that in the control group. The relatively low 12/16 NID in the control group was chosen because of the time of the onset of the study the NID in the devices was programmed conventionally ‘in the box’ with a 12/16 NID and thus an additional detection delay of 3 s during capacitor charging.

Finally, the device used in the Protect group was presented as a ‘low-cost’ device with a 30–40% reduction in cost as compared with conventional biventricular ICDs. A cost-effectiveness
evaluation of this ‘low-cost’ device would be of interest in the actual economic situation.

The RELEVANT study has important clinical implications showing that a prolonged NID may significantly reduced the appropriate VA therapies, especially by the fact that self-terminating VAs are not treated too rapidly without increasing the risk of syncope but also with the dramatic decrease in inappropriate therapies. These important results have to be confirmed.

Figure 1 (A) Example of a ventricular fibrillation lasting 9 s with spontaneous termination (arrow). The purple points represent the ventricular rhythm with a ventricular cycle of 250 ms (240 b.p.m.); the blue squares represent the atrial rhythm with an atrial cycle of 915 ms (55 b.p.m.) with a ventriculo-atrial dissociation. (B) Atrial and ventricular intracardiac EGMs showing the self-termination of the ventricular fibrillation (yellow arrow) and the restoration of the synchronization of the paced atria and the paced ventricles (green arrow).
in a real randomized trial. Concerted efforts should be made to limit the number of inappropriate shocks. With conventional device programming numerous therapies considered as appropriate are in reality clinically unjustified therapies. The future would probably be a haemodynamic monitoring by the device itself allowing treatment only in poorly tolerated VAs. While waiting for this generation of intelligent devices and as many devices are not reprogrammed after implantation, we may presently propose to the manufacturers to program less conservative arrhythmia detection ‘in the box’ for an accurate positioning of the cursor between sensitivity and specificity on a clinical and not a technical basis.

Conflict of interest: none declared.

References