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Editorial

Adherence to optimal ICD programming: an unresolved issue

La adherencia a una programación óptima del DAI: una asignatura pendiente

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Implantable cardioverter-defibrillators (ICDs) have been demonstrated to improve survival in patients with or at risk of malignant ventricular arrhythmias and represent the standard of care for their treatment.[1] These devices work by delivering antitachycardia pacing (ATP) and/or shocks. Shocks are associated with increased mortality, hospital admission for heart failure, and impaired quality of life.[2] Therefore, after ICD implantation, optimal programming is essential, the main aim being to reduce unnecessary or inappropriate therapies.

Optimized ICD programming has been much studied since the 1990s. Several studies have contributed to fine-tuning ATP programming and the use of criteria and algorithms for discriminating supraventricular tachycardias. These have resulted in, respectively, a reduction in appropriate shocks and inappropriate ICD therapies.

Four large, randomized studies (EMPIRIC[3], MADIT-RIT[4], ADVANCE III[5], and PROVIDE[6]) and 2 prospective observational studies (PREPARE[7] and RELEVANT[8]) have demonstrated that long-interval and/or high-rate detection programming reduce the number of therapies, both appropriate and inappropriate. The use of high-rate detection (over 200 bpm) was even associated with a reduction in mortality.[4] A meta-analysis of these studies showed that such programming strategies achieved a 30% reduction in all-cause mortality, compared with conventional programming, attributable essentially to a reduction in inappropriate shocks.[9] They mostly included patients who had received an ICD as primary prevention. Only the ADVANCE III study included secondary prevention implants and demonstrated an overall reduction in appropriate and inappropriate therapies. In it, they used prolonged detection (30 of 40 intervals), a detection window over 188 bpm, and ATP before or during capacitor charging. The importance of these results led to the publication, in 2015, of a consensus document on optimal ICD programming from the arrhythmia scientific societies *Heart Rhythm Society, European Heart Rhythm Association, Asia Pacific Heart Rhythm Society* and *Latin American Heart Rhythm Society* (previously SOALECE).[10]

Despite all the scientific evidence, very little information is available on the safety and effectiveness of optimal programming in real-world clinical practice. Likewise, the adoption of such programming, the factors that determine it, and how adherence to it could be improved have all been the subject of study. In the field of pharmacological treatment of heart failure, a significant delay (of many years, even) has been observed between the scientific evidence generated and clinical practice.[11] Both aspects are of great practical interest: first, we need to know if the results obtained in clinical trials are reproducible in real-world clinical practice, and second, there is little point in having good results in trials if the evidence generated is not adopted. Determining which factors lead to greater adoption could improve this.

Large-scale observational registries and the studies derived from them can help answer these questions. In addition, remote monitoring of patients with ICDs gives detailed, up-to-date information on device programming, the incidence of arrhythmias, and ICD therapies and their effectiveness, making it a very useful tool for conducting clinical studies. A good example of this is the SCOOP platform (Scientific COOperation Platform) which, until 2016, used the database from the remote monitoring system CareLink (Medtronic, Spain), along with clinical variables obtained from clinical practice. This platform allowed the generation of clinical evidence in the field of implantable cardiac devices, through efficient scientific collaboration. Participating investigators were allowed access to these data for scientific purposes, following agreed procedures for application, evaluation, and responsibility for the analysis. Within SCOOP, the UMBRELLA study was conducted: an observational multicenter Spanish study whose main objective was to analyze the incidence of arrythmias in the population with ICD and describe the prognosis for arrhythmias and mortality.[12]

In a recently-published article in *Revista Española de Cardiología,* Loughlin et al. present a study derived from this platform in which they analyzed, using a retrospective observational design, the adherence to a programming strategy as described in ADVANCE III, the predictors of such adherence, and its effect on the incidence of

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therapies compared with conventional programming.[13] Changes in the adoption of ADVANCE III-style programming were evaluated in relation to the publication of that study (May 2013), the implementation of a training campaign for the manufacturer's technicians who provide assistance with implantation (January 2015), and the publication of the aforementioned consensus document[10] (November 2015).

The study included 3528 patients. Over the whole study period, ADVANCE III programming was used in 20.3% of these patients, reaching 44% at the end. Adoption of this programming in real-world clinical practice was limited and slow, despite the evidence of clinical benefit. It increased mainly after the publication of the study (3.8% per trimester, with mean adherence of 31.8%) and, to a lesser degree, after the training campaign (2.2% increase and adherence of 62.6%) and the publication of the consensus document (2.5% and 45.2%, respectively). The predictors of adherence were implantation of an ICD with nominal ADVANCE III programming, implantation by an electrophysiologist, and use as secondary prevention, while implantation of a dual-chamber or cardiac-resynchronization therapy ICD was associated with lower adoption of this programming. Regarding the effect on incidence of therapies, the ADVANCE III programming strategy was associated with an overall reduction of 23% (34% for inappropriate shocks, 21% for appropriate ATP, and 46% for inappropriate ATP), with no difference in appropriate shocks.

We must congratulate the authors as this is the first study that provides data from real-world clinical practice on the effectiveness of ADVANCE III programming, and also for the originality of the analysis of predictors of adoption of this programming. These congratulations should be extended to the SCOOP and UMBRELLA investigators for the multiple published studies generated. These have provided useful information for improving ATP programming and reducing shocks, such as the use of multiple ATP sequences or one ATP sequence before and during charging for the treatment of rapid ventricular arrhytmias.[14]

The study by Loughlin et al. is not free from limitations, most of which are inherent to its retrospective design. First, it analyzed the adoption of ADVANCE III programming at the first ICD implantation or exchange, but it did not assess changes in programming during follow-up. Another limitation, which may have influenced the incidence of shocks, is that the authors did not analyze the types of ATP therapies used in each study group. In addition, it is unknown if some patients received programming more akin to the MADIT-RIT study,[4] particularly rate detection over 200 bpm, which could have reduced adherence to ADVANCE III programming. The time elapsed between publication of the expert consensus document and the end of patient inclusion in the UMBRELLA study (5 months) was very short to evaluate its effect on adopting the recommendations. Last, it does not provide information on the effect on clinical outcomes, such as the incidence of syncope during therapies, hospital admissions, mortality, and quality of life.

IS THE EVIDENCE FROM CLINICAL TRIALS ON OPTIMIZATION OF ICD PROGRAMMING REPRODUCIBLE IN CLINICAL PRACTICE?

In addition to Loughlin et al., other authors have analyzed the degree of adherence and speed of uptake of programming strategies with demonstrated benefit in clinical trials. All have in common that they show a slow, limited uptake, albeit progressive and more marked in the year after the study was published.[15–17] The publication of the consensus document and the training campaigns for the technicians that assist with implantation had little effect in the short- to mid-term. Varma et al. analyzed the adoption of programs used in the MADIT-RIT study[4] or recommended in the expert consensus in a cohort of patients with ICD undergoing remote follow-up on the platform Latitude (Boston Scientific, USA). Adherence increased mainly in the year after publication of the study (12.6%), but the subsequent increase was small (< 6% in the following 5 years).[17] Ananwattanasuk et al. observed that only a third of the population studied had an ICD programmed in line with the recommendations in the expert document.[16]

DO WE INCORPORATE THE EVIDENCE INTO OUR CLINICAL PRACTICE?

Determining the predictors of adoption of optimal programming may help to drive measures to improve adherence. This was one of the most original and interesting take-away messages from the work by Loughlin et al., who found such predictors to be the inclusion of programming evidence as nominal parameters in the devices, implantation by electrophysiologists, and use as secondary prevention.[13] In the study by Varma et al., the predictors were younger age, female sex, and follow-up in a tertiary or university hospital.[17] Implantation by an electrophysiologist and the availability of a heart failure unit were predictors of adoption of the ICD indications from the IMPROVE HF study.[18] These nonclinical predictors, which were the same in several studies, could reflect differences in training, access to clinical guidelines and consensus documents, as well as the availability of instruments to ensure the recommended care for all patients, and they should be taken into account when planning care for patients who are candidates for ICD.

CAN WE IMPROVE ADHERENCE TO OPTIMAL PROGRAMMING?

To improve health outcomes, we need not only research and scientific output, but also the incorporation of scientific evidence into clinical practice. In the field we are concerned with, the consequences of inaction could be serious, given the clinical implications of ICD shocks.

As has been seen before, passive promotion of the evidence, such as the publication of clinical trials or clinical guidelines is not very effective at improving adherence,[13,15–17] supporting the need for active promotion.

One of the active strategies, as Loughlin et al. showed, is for manufacturers to incorporate the evidence from large clinical trials and the consensus recommendations into the nominal programming settings on the ICD.[13] Some companies have followed this policy for years and the rest should adopt this practice. This measure would affect first implantations and exchanges, although it would not solve the need for programming adjustments as new evidence is included in the knowledge base. Varma et al. observed a reprogramming rate during clinical follow-up of $< 2\%$, which suggests that programming optimization is not considered a priority for patients who have not received ICD therapies.[17]

Other strategies should be based on providing feedback to physicians about adherence to the recommendations for optimal programming, both at implantation and at patient follow-up. The implementation of campaigns aimed at training and raising awareness in the technicians who assist with implantation increases adherence, albeit modestly.[13] Direct feedback to physicians has been shown to be more useful. In the Shock-Less study, this strategy achieved a 20% increase, which translated to a 28% reduction in all shocks.[19] Last, the data from remote monitoring of devices can also identify deviations from optimal programming leading to reprogramming. This requires active periodical review by the clinic staff who perform remote follow-up, although the manufacturers could facilitate this process as part of their service.

We must ask ourselves how strict we should be when applying the evidence on optimal ICD detection programming. Each of the large studies on this subject was performed with devices made by different companies, with different sensing and detection modes. Thogersen et al. reported that most patients who did not receive an appropriate shock for an episode of ventricular fibrillation had an ICD that had been programmed according to the extrapolation of evidence obtained from studies performed with ICDs from other companies.[20] This finding highlights the need for studies that evaluate the risks and benefits of applying detection parameters based on evidence from a study performed with an ICD from one manufacturer to another. Thus, although the consensus document provides general recommendations on programming, and for some ICDs these are extrapolations from evidence obtained with devices from other manufacturers, it is recommended to program each ICD in accordance with the evidence of demonstrated benefit in ICDs from the same manufacturer.

In conclusion, for a greater potential benefit from ICD implantation, we need not only the correct indication, but also optimal programming. In light of the studies that show that optimal ICD programming reduces shocks as well as mortality in real clinical practice, we need greater adherence to optimal programming. For this, we need active measures and research aimed at demonstrating their usefulness.

CONFLICTS OF INTEREST

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