Current Practice in Italy of VF Testing at Implant: What Do We Know and Where Do We Go From Here?

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What Do We Know?

The standardized requirements for cardioverter defibrillator (ICD) implantation, with or without cardiac resynchronization therapy (CRT), include defibrillation testing (DT), which consists of the induction and termination of ventricular fibrillation (VF). This procedure has been followed from the early days of ICD therapy in order to assess the reliability of an implanted ICD device and to measure the defibrillation threshold. Effective DT is considered mandatory in accordance with the rules of good clinical practice.

Nowadays, since the implantation procedure for ICDs has become markedly simplified and the surgical risk is very low, DT can be considered to be the most critical part of the implantation procedure itself. Although the risk associated with DT is usually low, serious complications may nonetheless occur as a consequence of this practice. Complications include transient ischemic attack or stroke, cardiopulmonary arrest due to refractory VF or pulseless electrical activity, cardiogenic shock, embolic events, and death. This knowledge comes from small single-center retrospective surveys [1] and from anecdotal experience. However, in the absence of data from large populations enrolled in multi-center registries, the real magnitude of intra-operative complications related to DT is still largely unknown.

Although the standardized approach to ICD implantation still includes a VF induction test, data coming from real-world experience suggest that an increasing number of first-implantation procedures are performed without

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any induction test. It seems that some physicians are concerned about practicing DT in patients considered to be at very high clinical risk. For example, in two single-center populations, Russo et al. [2] reported a lack of induction testing in 4.7% and Pires et al. [3] in 24% of patients. The reasons for omitting induction testing included intraoperative hypotension or hemodynamic instability, known cavity thrombus or previous inadequate anticoagulation therapy, recent cardiovascular accident, severe comorbidities, and the absence of anesthesia support.

The *Associazione Italiana di Aritmologia e Cardiostimolazione* (AIAC) recently conducted a systematic nation-wide retrospective survey to determine how often and for what reason intra-operative DT was or was not performed, and the complication rate related to induction testing.

An ad-hoc questionnaire was sent to 343 centers implanting ICDs (listed in the database of the Italian ICD Registry of the AIAC), which essentially represents all of Italy's implanting centers. The ICD implantation data collected by the Italian ICD Registry of the AIAC is formatted according to the recommendations of the European ICD Registry (EURID).

The survey was limited to patients undergoing initial ICD implantation during the year 2005. Questionnaire and data collection were carried out through the World Wide Web from June to October 2006. Participating centers were asked to communicate their data regarding the total number of ICDs (including those with CRT features), number of implantations in which DT was performed intraoperatively or before discharge, and number and type of DT-related complications. DT was defined as at least one induction of VF. DT-related complications were considered those life-threatening events occurring immediately after VF induction.

Of the 8,820 first ICD/CRTs implanted in Italy during 2005, data on 7,857 (89%) implantations (38% of whom CRT) performed in the 229 centers that participated in the survey were analyzed. Of these, 2,356 (30%) implantations did not include an induction test (Table 1). In 35 (15%) centers, an induction test was administered in < 25% of the patients, while in 136 (59%) centers it was done in > 75% of the patients. In a multivariable analysis of a subset of 1,206 patients from 107 centers, CRT device (OR 1.82) and primary prevention (OR 1.47) were independent predictors of the decision to not administer DT. However, all together, clinical variables accounted only for 35% of the total variance, and the remaining 65% was probably unrelated to clinical factors (Table 2). Life-threatening complications as a consequence of the induction test were reported in 22 (0.4%) patients: four deaths (0.07%), eight cardiopulmonary arrests requiring resuscitation maneuvers (0.15%), six cases of cardiogenic shock (0.11%), three strokes (0.05%), and one pul-

Table 1. Principal findings

Centers invited to participate	343 (%)
Centers that participated	229 (67)
Total number of first-implant procedures	7,857
With intraoperative defibrillation test	5,501 (70)
Without intraoperative defibrillation test	2,356 (30)
Total number of complications related to defibrillation test	22 (0.4)
Death	4 (0.07)
Cardiopulmonary arrest requiring resuscitation	8 (0.15)
Cardiogenic shock	6 (0.11)
Stroke	3 (0.05)
Pulmonary embolism	1 (0.02)

Table 2. Univariable and multivariable predictors of the decision to not perform the induction test in a subset of 1,206 patients

Factors	**Percent**	**Univariable Odds ratio (95% CI)**	***p***	**Multivariable Odds ratio (95% CI)**	***p***
Age (70	43	1. 31(1.03–0.67)	0.03	1.29 (0.99–1.67)	0.06
Male gender	87	1.22 (0.86–1.72)	0.25	–[a]	–
CRT device	19	2.01 (1.50–2.68)	< 0.001	1.81 (1.30–2.53)	< 0.001
Primary prevention	45	1.65 (1.30–2.09)	< 0.001	1.50 (1.14–1.97)	0.003
Ejection fraction (30%	51	1.68 (1.30–2.16)	< 0.001	1.30 (0.97–1.72)	0.07
Dilated vs ischemic	47	1.42 (1.12–1.80)	0.004	–[b]	–
NYHA class > 2	23	1. 96 (1.46–2.63)	< 0.001	–[b]	–

[a]Male gender was not analyzed in the multivariate model because it was not significant in the univariable analysis
[b]Dilated vs ischemic and NYHA class were not inserted in the multivariable model as these resulted were covered by the parameter CRT device
CRT, Cardiac resynchronization therapy; *NYHA*, New York Heart Association

monary embolism (0.02%). Failure of an ICD defibrillation test, and thus the need for a backup external defibrillator, was 2.7%, which determined a system revision (i.e., additional lead insertion, etc.) in 2.3% of patients.

This nation-wide survey was the largest ever performed and covered 89% of the overall first-implantations in Italy during 2005. The main finding was that, in real-world clinical practice, DT was not administered in 30% of

patients, and in most of these cases there was no legitimate reason for the omission. Nonetheless, DT is still considered part of the standard procedure of ICD implantation. There was wide heterogeneity between centers and more than a quarter of Italian centers did not administer DT in ≥ 50% of their patients. These figures, which were much higher than those expected from the literature [2, 4], not only reflect the spontaneous non-conformist opinions of several physicians they also go beyond the current recommendations of ICD manufacturers. Given the large number of physicians who do not include DT during ICD implantation, the decision requires explanation and merits specific actions in response.

One explanation for the limited use of DT is the increasing role of primary prevention strategies [5, 6], which address patients with very low ejection fraction and advanced NYHA class [7]. The selection of sick patients due to expanded ICD indications was recently confirmed in a comparison of USA and Italian practices [8]. However, all together, the clinical variables accounted only for 35% of the total variance whereas the remaining 65% was probably unrelated to clinical factors. Therefore, the main reasons for the violation of current standards in so many patients seem to be, on the one hand, the concern for severe complications related to intraoperative DT and, on the other, the conviction of a small risk of death due to failure of the ICD to interrupt VF during long-term follow-up.

In the Italian survey study, the DT-related life-threatening complication rate was not negligible, accounting for 0.40% of cases, considering that DT in the analyzed cohort of patients was preferably administered to less sick patients (Table 2). The complication rate might have been even higher if the patients with severe heart failure and very low ejection fraction were not preventively excluded from undergoing DT. In the literature, there are a few reports based on small studies concerning intraoperative complications. A report [1] on 440 consecutive single-center ICD implantations showed 0.2% perioperative deaths, 0.5% difficulty in defibrillation with requirements for more than three external shocks, and 0.7% perioperative ischemic attack. In another single-center study [2], consisting of 835 ICD implantations, there were three (0.35%) perioperative deaths (within 30 days of implant). It has been reported that shocks during DT may cause hemodynamic compromise [9], especially in patients with severe heart failure, as are candidates for CRT. Moreover, anesthesia has a cardiac-depressive effect in the presence of VF induction [10]. The clinical conditions of patients undergoing implantation may be worse but might improve later with CRT, thus decreasing the risk of complications related to DT. For example, a DT delayed up to 2 months after

CRT device implant, when the patient's clinical condition has improved due to CRT, showed effectiveness without compromising safety [11].

Few data are available on the risk of death due to the failure of the ICD to interrupt a VF during long-term follow-up. Sudden death in patients with ICD is reported to range from 1.8 to 2.6% during 1–3 years of follow-up [12–14]. Analysis of the mechanisms of sudden death, with data retrieved from ICD diagnostic memory, showed that only a quarter of the above-mentioned cases could be attributed to shock failure during VF [13]. Therefore, it can be assumed that the sudden death rate potentially attributable to shock failure ranged from 0.45 to 0.65% during 1–3 years of follow up. This percentage is very similar to the percentage of intra-operative deaths following VF induction during implantation. There are no data that specifically demonstrate increased mortality among patients with high DT thresholds at implant. In a recent study [3], both the success of ICD therapy and sudden-death-free survival were similar in patients who had defibrillation threshold measurement, safety margin testing, or no testing.

Where Do We Go from Here?

Is it time to change the current standard of performing DT at the time of ICD implantation? The question has been previously raised by several experienced clinicians [2–4, 14, 15]. However, there is no evidence-based answer yet. The reasons for and against DT are summarized in Table 3. The clinical impact of DT vs. no DT will remain unclear until the not-negligible intraoperative complication rate is weighted against the long-term potential benefit of DT. Long-term follow-up data regarding the safety and efficacy of ICD implantation in large groups of patients in whom DT is not performed are needed. Until this information becomes available, DT should be considered as a standard practice. Data from the literature and from the present study support the need to carry out large multicenter studies and emphasize the urgent need for precise recommendations from the relevant clinical specialties.

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Table 3. Advantages and disadvantages of performing DT at the time of implant

Reasons in favor of induction	Reasons in favor of noninduction
• Standard practice for ICD implant • Most device safety studies required DT at implant • DT allows the choice of corrective measures at implant in case of high threshold • DT ensures that the system provides appropriate sensing of VF • DT may include the defibrillation threshold evaluation for better ICD programming	• No data specifically demonstrate increased mortality among patients with high DT thresholds • A quite small probability of a high threshold and a failed implant with current technology • The nature of the defibrillation threshold is probabilistic and repeated shocks below threshold can be effective • The shocks may cause hemodynamic compromise • The cardiac depressive effect of anesthesia in addition to VF induction • In the great majority of patients receiving an ICD, the initial spontaneous life-threatening arrhythmia is VT and not VF; thus, a DT at implant imposes an additional risk that most patients would not otherwise have in their lives • Patients at implant may have worse clinical conditions that could improve later with CRT, thus decreasing the risk of complications related to DT • In one retrospective analysis, success of ICD therapies and sudden-death-free survival were similar in patients who had defibrillation threshold testing, safety margin testing, and no testing

ICD, Cardioverter defibrillator; *DT*, defibrillation testing; *VT*, ventricular tachycardia; *VF*, ventricular fibrillation; *CRT*, cardiac resynchronization therapy

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