Timing of defibrillator implant after acute myocardial infarction: what’s new?

Massimo SantINI* and Carlo Pignalberi

Cardiovascular Department, S. Filippo Neri Hospital, Via Martinotti 20, 00135 Rome, Italy

Received 16 November 2010; accepted after revision 22 November 2010; online publish-ahead-of-print 24 December 2010

This editorial refers to ‘Clinical practice of defibrillator implantation after myocardial infarction: impact of implant time: results from the PreSCD II Registry’ by H. Völ ler et al., on page 499.

Cardiovascular disease is the second major cause of death in western countries after cancer. About half the patients with acute myocardial infarction (AMI) die suddenly due to malignant ventricular arrhythmias.1 The study of AMI patients conducted in the 1970s and 1980s has shown that the risk of sudden death was increased between 6 and 12 months after necrosis, particularly in patients with impaired left ventricular systolic function.2,3 Technological advances and the use of new drugs introduced in recent years have considerably reduced the incidence of sudden death, mainly by protecting the myocardium and preserving its contractile function. In the last 10 years, the widespread use of implantable cardioverter defibrillators (ICDs) has led to a significant decrease in the overall mortality through almost complete abolition of arrhythmic death. Patients with ischaemic or idiopathic cardiomyopathy, left ventricular ejection fraction (LVEF) ≤35%, and clinical symptoms of heart failure are candidates for ICD implantation for primary prevention. An ICD should be implanted for secondary prevention in patients who have experienced malignant ventricular arrhythmias or cardiac arrest.4–6 At present, however, there is a significant discrepancy between the guidelines and clinical practice in selecting the candidates for ICD implant; in addition, the debate on device implantation timing is still ongoing.

Völ ler et al.7 attempt to give an answer to these two controversial topics. The Prevention of Sudden Cardiac Death II (PreSCD II) registry has enrolled a large population of 10 612 patients in 19 rehabilitation centres in Germany to evaluate the clinical practice of ICD therapy in patients with AMI who are the potential candidates for ICD implant. The authors divided the population into three groups according to LVEF: Group 1 included 269 patients with LVEF ≤30%, Group 2 has 727 patients with LVEF 31–40%, and Group 3 included 1148 patients with LVEF >40%. After 3 years of follow-up, an ICD was implanted in only 6.9% of patients. Specifically, in Group 1 (in which, according to the guidelines, all patients should receive an ICD) implantation was performed in only 31.7%; similarly, in Group 2, a much higher proportion of device implantations than the observed 7% was expected. In patients who received an ICD, all-cause mortality was reduced by 44%. An 11-month interval between the occurrence of AMI and ICD implant was selected as a cut-off point: above this limit, mortality from all causes was significantly lower.

Two important points come out from the results of this registry. First, implantation of an ICD was performed in less than one-third of patients who met the criteria recommended by the guidelines. In addition, the greatest benefit from ICD therapy was seen only in patients in whom implantation was performed relatively late after the occurrence of AMI.

The adherence to guidelines is a topic widely debated in the literature and is relevant in all areas of medicine, particularly in situations involving the use of expensive treatments or devices, especially if their cost is not diluted over time. Such therapies appear more expensive, but actually they may be less expensive than other procedures that are not associated with significant initial costs, but incur a constant expenditure over time.8 In the registry by Völ ler et al., the main causes of poor adherence to the guidelines were patients’ refusal to have an ICD and the reluctance of treating physicians to refer the patients for ICD implant (~64% of all cases). Other reasons (numerically less relevant, but conceptually more significant) were those related to poor physical condition of patients, reduced life-expectancy, and old age.

The main reason for criticizing this attitude is the observation that older patients with compromised left ventricular systolic function, and the presence of important co-morbidities, including renal failure, are those who derive the greatest benefit from an ICD.9 This concept has been well reflected in the editorial by Moss10 published ~10 years ago: ‘The sickest patients benefit the most’, but, obviously, this concept has not yet been fully implemented in clinical practice. It is important to note, however, the efforts of the scientific community to identify the clinical features that are used to justify withholding ICD therapy. Even more important,
However, is to identify the reasons related to the physicians’ resistance to use an ICD, the same resistance that is then transmitted to patients through a sceptical description of this treatment strategy. Thus, in the present registry, this aspect represents almost 64% of causes of non-adherence to the guidelines. In the recent Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF) registry—conducted in the United States, among 7221 patients who met the eligibility criteria for ICD implant, only 50.7% actually received an ICD. The main cause of non-adherence to the guidelines was old age; other reasons were the black race, lack of insurance, hospitalization in non-specialized facilities for the treatment of heart failure, and lack of electrophysiologists among the medical staff. What is more important than the non-adherence to the guidelines, however, is the evaluation of the physicians’ opinion in relation to ICD implant.

In a very recent study on physicians’ knowledge and attitudes regarding ICD therapy, although cardiologists and primary-care physicians were all aware of the ICD guidelines, their knowledge on specific issues, such as the use of ICD in women and some racial minorities, was not so strong. Two particular aspects have been discussed: age and cost. Among the interviewed physicians, 76% believed that an ICD could be of benefit in patients ≥ 70 years, but only 49% thought an ICD would be beneficial in patients ≥ 80 years. This result is linked to the medical assessment (age is considered to be associated with severe co-morbidity, impaired functional status, and cognitive function) and ethical judgment (issues around quality of life and death). These aspects, however, have yet to be debated widely from the medical and human point of view. Finally, in relation to the cost of ICD therapy, we have previously emphasized the long-term benefits of a large single initial investment. However, in the current climate of cost restraints and the increasing role of the government involvement in healthcare financing, many strategic choices that lead to a reduction of adhesion to guidelines are understandable.

The second issue raised in the study by Völker et al. is the correct timing of ICD implantation after AMI, which is currently the subject of intense debate. In a subgroup analysis in patients enrolled in Multicenter Automatic Defibrillator Implantation Trial (MADIT) II study, after dividing the patients into four subgroups according to time elapsed between AMI and ICD implant, the benefit from ICD therapy was very small in the first quartile (implant performed <18 months after AMI), while it was substantial and comparable across the other groups. The reasons for these unexpected results could be manifold: younger median age, better left ventricular systolic function, higher utilization of beta-blockers, and a smaller proportion of patients with QRS duration >120 ms among others. In addition to the arbitrary selection of the time cut-off for analysis, other factors may explain this unexpected result: the very low mortality rate at 1 year, the presence of selection bias made by the exclusion of patients at the highest risk, and the widespread use of electrophysiological testing. Furthermore, patients with AMI <1 month were excluded.

The Defibrillator IN Acute Myocardial Infarction Trial (DINAMIT) study, which evaluated the effectiveness of early ICD implantation (6–40 days after AMI), has failed to demonstrate the efficacy of ICD therapy to reduce total mortality. Although there was a significant reduction of arrhythmic death in the ICD group, this benefit has been offset by higher mortality from non-arrhythmic causes. The results of the present study confirm these findings, despite a longer cut-off period in the registry (11 months). Based on the results of the DINAMIT trial and the previous studies, the current guidelines recommend a delay of 40 days as the minimum time prior to ICD implantation. It is possible that some patients who had died at this early stage, even from arrhythmic causes, would have died anyway from other causes even if the arrhythmia risk has been addressed. For that reason, to date, there are no sufficient data to justify early ICD implant after AMI.

However, a cohort of patients at a high risk of sudden death in the very early phase after AMI can be identified—patients who experience episodes of ventricular tachycardia or ventricular fibrillation with a rate > 10% during hospitalization for AMI. In the VALsartan In Acute myocardial infarction Trial (VALIANT), 1067 out of 14 609 patients had a major arrhythmic event (sudden death or resuscitated cardiac arrest). The first month post-AMI was the period with the highest risk of sudden death (1.4%, with a significant drop to a relatively constant rate of 0.14–0.18% per month thereafter). At that time, 90% of all events occurred, with the highest rate (2.3% per month) in patients with depressed LVEF (30% or less). A very alarming observation was that 83% of sudden deaths occurred in the first 30 days after hospital discharge.

What is the importance of these observations? These findings point to the fact that, at the moment, routine ICD implantation immediately after AMI in patients who meet the indication of guidelines, is not cost-effective, but the presence of an important cohort of patients, mainly characterized by significant left ventricular dysfunction, that are at a high risk of sudden death in the first 30 days after AMI warrant a therapeutic strategy as a bridge until the arrhythmic risk is reduced or ICDs are implanted. The alternative to ICD implantation is the use of certain drugs on top of the conventional therapy. In the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival (EPHESUS) study, eplerenone (a selective aldosterone blocker) has been found to reduce cardiovascular events in the first 30 days after AMI, starting 10 days after randomization. Specifically, in the first month after AMI, eplerenone reduced all-cause mortality by 31% and sudden death by 37%. A more significant reduction in sudden death by 58% was observed in patients with impaired LVEF (<30%). Alternatively, an automated external defibrillator (AED) could be provided for high-risk patients for the use by the family members after appropriate training. However, the extensive use of this device did not provide any exciting result: in a large randomized study of 7001 patients with previous anterior AMI who were not candidates for ICD implant, no difference was found between AED and standard cardiopulmonary resuscitation and call for emergency medical services. Finally, the use of the wearable cardioverter defibrillator (WCD) appears a promising strategy. It could be an alternative approach to protection against sudden death in high-risk patients during the first month post-AMI, bridging them to the appropriate time for ICD implantation. In a large, recently published German series, including 354 patients who had used WCD between 2000 and 2008 for a period of 3
months post-AMI, 246 arrhythmic events in 27 patients were efficiently terminated.

In conclusion, the registry by Völler et al. highlights two important aspects in the management of patients with recent AMI at risk of sudden death. In clinical practice, it is necessary to maintain a good adherence to the ICD guidelines. In addition, it is important to improve the knowledge of both cardiologists and emergency physicians on the benefits of ICD therapy, since it represents the most effective therapy against malignant ventricular arrhythmias. The second critical point is the management of risk of the arrhythmia in the first month after AMI. Even if there is no scientific evidence to support ICD implantation in the very early post-AMI phase in patients at risk of sudden death, there is certainly a clear need to provide them with an effective protection until an ICD is implanted or the arrhythmia risk is significantly reduced.

Conflict of interest: M.S. has been an investigator and speaker for Medtronic Inc., St. Jude Medical and Biotronik. C.P. has been an investigator for Medtronic Inc.

References