Timing of implantation of cardioverter-defibrillator after acute myocardial infarction

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This editorial refers to ‘Relation between time from myocardial infarction to enrolment and patient outcomes in the Multicenter UnSustained Tachycardia Trial’ by S.M. Al-Khatib et al., on page 1112.

Current guidelines recommend prophylactic implantation of cardioverter-defibrillator (ICD) in patients who are in functional class II or III and have a left ventricular ejection fraction (LVEF) ≤ 35% and in those in functional class I and LVEF ≤ 30%, when assessed at least 40 days after acute myocardial infarction (AMI). These guidelines are mainly based on three randomized, prophylactic ICD trials, which showed the mortality benefit of ICD therapy compared with standard medical treatment by using only functional class and LVEF as pre-defined inclusion criteria for randomization. Two other trials which used reduced heart rate variability, the Defibrillator in Acute MI Trial (DINAMIT), and elevated heart rate or presence of non-sustained ventricular tachycardia, Risk Stratification Improves Survival trial (IRIS) in addition to reduced LVEF, and which enrolled patients within 40 days after AMI, could not demonstrate the benefit of ICD implantation early after AMI. These partly controversial results have raised some questions regarding the optimal timing of assessment of the candidacy for ICD implantation after AMI, especially because there is evidence that a high proportion of sudden cardiac deaths occur within the first weeks (<40 days) rather than late after AMI.

There are many potential explanations for the discrepant results of prophylactic ICD trials. It is evident that there is a lot of variability in the risk profiles of patients at different time points after AMI. Ventricular remodelling is a well-known phenomenon occurring within the first weeks after AMI. A recent study showed that similar remodelling can also be observed in cardiac autonomic regulation and that the degree of this remodelling predicts future fatal or near-fatal arrhythmic events. These observations support the concept that risk profiling of patients should be performed relatively late, i.e. 6- to 8-week post-AMI, at the time when arrhythmic vulnerability is stabilized, rather than early after AMI. These time-dependent changes in arrhythmic risk profiles may also partly explain the negative results of studies using risk profiling of patients early after AMI. Secondly, the two negative studies used other risk stratification methods in addition to measurement of LVEF in their study designs. It is possible that these risk stratification methods do not specifically reflect an increased risk of arrhythmic events but are more closely related to increased risk of progressive heart failure. For example, reduced heart rate variability, elevated heart rate, and the presence of non-sustained ventricular tachycardia measured in the early convalescent phase of AMI were more closely associated with increased risk of non-arrhythmic than arrhythmic death in a large observational study. Therefore, both the DINAMIT and IRIS trials possibly included patients at high risk of non-arrhythmic death in their trials. Although the incidence of sudden cardiac death was reduced in these trials, the increased rate of non-arrhythmic deaths in the ICD group counterbalanced this beneficial effect. It can be speculated that patients included in the DINAMIT and IRIS trials were on the ‘slippery slope’, anyway, and died from non-arrhythmic death, probably due to progressive heart failure, despite the protection from fatal arrhythmic events. The other prophylactic ICD trials have shown that although patients with heart failure have an overall benefit from prophylactic ICD implantation, those receiving shocks have a substantially increased risk of non-sudden death.

Multicentre unsustained tachycardia trial (MUSTT) was a randomized ICD trial evaluating the ability of electrophysiologically guided antiarrhythmic therapy to reduce arrhythmic death or cardiac arrest in patients with LVEF ≤ 40%, coronary artery disease, and spontaneous non-sustained ventricular tachycardia occurring ≥4 days after AMI and ≤6 months before entry into the trial. A MUSTT substudy published assessed the relation between the time from AMI to enrolment and patient outcomes and examined the association between these outcomes and ICD therapy. The investigators used 6 months from AMI as a cut-off of early vs. late time period from AMI. The authors conclude that risk of arrhythmic death or cardiac death and all-cause death did not vary as a function of time from most recent AMI to enrolment, challenging the concept of larger benefit of late vs.
early risk stratification and ICD implantation after AMI. The obvious disadvantage of this study is the lack of information (due to a small number of patients) from the time period of first 3 months after AMI, which has been shown to be the most vulnerable period for sudden cardiac death. Thus, the question of optimal timing of assessment of candidacy for prophylactic ICD therapy remains open, even if invasive electrophysiological testing would be used for risk stratification.

The main focus of future research in this era will obviously be attempts to identify patients who are on the ‘slippery slope’ and show impaired recovery of ventricular and autonomic dysfunction as well as other features related to increased cardiac mortality during the early phase of AMI. Therapeutic options should then be searched for these patients in order to reduce the increased rate of early sudden death after AMI. The solution may be other than prophylactic ICD therapy.

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**References**


