The Challenge of Predicting and Preventing Sudden Cardiac Death Immediately After Myocardial Infarction

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The prediction and prevention of sudden cardiac death (SCD) in high-risk patients immediately after myocardial infarction (MI) remain daunting challenges.1 With widespread advances in the treatment of ST-segment elevation MI (STEMI) with primary percutaneous coronary intervention (PCI) and pharmacological therapy, sudden death and total mortality have decreased.2–4 However, mortality immediately after STEMI remains high in patients with impaired left ventricular ejection fraction (LVEF) with a particularly high risk of sudden death.2–4 Despite optimal therapy, the risk of SCD is highest in the first 30 days among patients with left ventricular dysfunction.4 Thus, earlier implementation of strategies for the prevention of sudden death immediately after a STEMI is needed.

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To identify immediate post-MI patients at high risk of sudden death, invasive and noninvasive risk stratification techniques have been evaluated.5 Risk stratification methods should provide information about the likelihood of SCD and non-SCD to identify potentially effective interventions, such as implantable cardioverter-defibrillator (ICD) therapy that prevents SCD and reduces mortality. LVEF has been established as a useful marker of increased mortality after MI, but it does not identify patients at increased risk of arrhythmic death relative to total mortality. Among the risk stratification techniques evaluated alone or in conjunction with LVEF to identify patients at high risk for arrhythmic mortality are spontaneous or induced ventricular arrhythmias, the signal-averaged electrocardiography, QT interval dispersion, microvolt T-wave alternans, increased QRS duration, baroreceptor sensitivity, and heart rate variability and turbulence.5 In patients with high rates of sudden death but low rates of nonsudden death, ICD therapy can provide effective and cost-effective therapy.6 In contrast, when used in patients with lower ratios of sudden to nonsudden death, the benefit of therapy is substantially diminished because these patients have a high mortality rate even if SCD is effectively prevented.6

The clinical utility of any risk stratification technique needs evaluation in appropriately designed and powered trials to determine whether an intervention reduces arrhythmic death and reduces total mortality. Multiple clinical trials randomizing several thousand patients have demonstrated that the ICD prevents sudden death and significantly reduces overall mortality among patients with left ventricular dysfunction due to ischemic heart disease.7–10 However, these trials have excluded patients with recent MI.7–10 By contrast, the trials assessing the role of the ICD in patients at high risk for SCD immediately after MI have failed to show survival benefits.11–17 The Defibrillator in Acute Myocardial Infarction Trial (DINAMIT) assessed the strategy of ICD use in a randomized controlled prospective study of 674 patients within 4 to 40 days after an index MI. All enrolled patients were receiving optimal pharmacological therapy and had LVEF ≥35% with markers of autonomic dysfunction. Only 27% of patients were treated with PCI. Although depressed LVEF and low heart rate variability identify patients with increased mortality risk, the trial did not identify any subsequent benefits from the use of ICD in these high-risk patients.11

The Immediate Risk-Stratification Improves Survival (IRIS) trial evaluated the strategy of early post-MI ICD implantation with randomization of 900 high-risk patients within 1 month of an MI with LVEF <40% on optimal medical therapy to this therapy.12 Primary PCI was used in 245 of these patients. Although the ICD group showed a significant reduction in arrhythmic mortality, this result was offset by an increase in nonarrhythmic death, similar to DINAMIT.11,12 In another prospective randomized trial, the strategy of home-automated external defibrillators use in high-risk post-MI patients failed to improve survival compared with conventional resuscitation methods.13 Although the short-term use of noninvasive vest defibrillation is a reasonable approach with high-risk post-MI patients, it remains to be evaluated in appropriately designed prospective trials.

Prior studies using invasive techniques for risk stratification with programmed ventricular stimulation (PVS) in the immediate post-MI period have also failed to demonstrate clinical utility.14–17 Recently, the Beta-Blocker Strategy Plus Implantable Cardioverter Defibrillator (BEST-ICD) trial evaluated the utility of PVS in patients at high risk of SCD within the first month after a STEMI, randomizing 143 patients on optimal medical therapy to ICD.17 Although a trend favored PVS-guided ICD therapy, no survival benefit was found in this trial.17

In this issue of *Circulation*, Zaman and colleagues evaluate an invasive strategy of early risk stratification with PVS and selective ICD implantation in 689 patients with induced ventricular tachycardia.18 Consecutive patients with LVEF...
<40% underwent invasive risk stratification with PVS. If sustained monomorphic ventricular tachycardia was induced, an ICD was implanted before discharge. At a median follow-up of 12 months, no significant difference was found in survival between those with LVEF >40% and those with LVEF <40% with and without inducible arrhythmias (P=0.879). In the subgroup of patients with LVEF ≤30% and no ICD (n=25), 9% mortality was found at median follow-up of 25 months. The authors conclude that early ICD implantation limited to patients with inducible ventricular tachycardia enables a low overall mortality in patients with impaired LVEF after STEMI treated with PCI. This article by Zaman is noteworthy because it represents the first primary prevention protocol as part of a regionalized PCI program. No excess mortality was noted with early ICD implantation, and mortality was low compared with previously published trials. In contrast to prior studies in patients with recent MI, in which a minority of patients had PCI, this study had 95% of patients revascularized with this technique. Similar to prior trials using both noninvasive and invasive risk stratification techniques followed by ICD therapy, in patients immediately post-MI the primary end point of improved survival was not reached.11–17

Multiple potential reasons exist for this lack of survival benefit with early risk stratification and ICD intervention in post-MI patients. It is possible that ICD truly does not reduce arrhythmic death and improve total mortality in this patient population as the available data from these trials indicate.11–18 It is also possible that ICD therapy could demonstrate a survival benefit if risk stratification techniques were better able to identify patients at risk of arrhythmic death compared with death from other causes. The ICD may decrease arrhythmic death but increase total mortality because of deleterious effects of implantation or shock therapy. These explanations are not mutually exclusive, and multiple factors may contribute to a lack of demonstrated benefit. Additional factors that might contribute to the lack of demonstrated benefit are related to limitations of the study designs and power. The studies assessing ICD therapy immediately after MI enrolled several hundred patients and may have been underpowered to detect a true mortality benefit.11–18 Demonstration of a statistically significant equivalence to within 1% in survival between patients with LVEF <40% with and without an ICD in the article in this issue of Circulation would require 3644 patients in each arm.18 Furthermore, in the current study, all inducible patients with ejection fraction <40% received an ICD. Thus, even if adequately powered to detect a difference in survival in the 3 arms of the study, the absence of randomization would limit interpretation of the results. Without a true control group of patients with LVEF <40% and inducible ventricular tachycardia not treated with an ICD, assessing whether the therapy had a favorable, adverse, or neutral effect would be difficult.

On the basis of the results of the trial in this issue of Circulation, as well as on the basis of others evaluating ICD implantation in high-risk patients immediately after MI, insufficient evidence exists to support routine risk stratification to guide ICD implantation. It is evident that additional research is needed with appropriately designed and powered studies to identify risk stratification and intervention strategies to prevent SCD and improve survival immediately after MI. In the meantime, clinicians should optimize and individualize therapy in the immediate post-MI patient while carefully considering the risk of sudden death and the competing risk of mortality from other causes.

Disclosures
None.

References


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