Survival of the Fittest
Evolution of Left Ventricular Ejection Fraction After Acute Myocardial Infarction

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Sudden cardiac death (SCD) resulting from cardiac arrest remains the leading cause of cardiovascular mortality worldwide and accounts for >250,000 deaths annually in the United States.1-4 The majority of cardiac arrests occur in patients with a prior myocardial infarction (MI) at a rate ~5 times that of the general population.1 Studies evaluating the time dependence of mortality immediately after an MI have consistently demonstrated that the greatest risk for SCD is in patients with impaired left ventricular (LV) ejection fraction (LVEF).5-7 Despite revascularization and widespread use of β-blockers, angiotensin-converting enzyme inhibitors, statins, and antiplatelet agents, the risk of SCD remains highest in the first 30 days in these patients.5-7 On the basis of these observations, strategies for the prevention of SCD need to be implemented early after an MI in high-risk patients.

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Although depressed LVEF identifies patients with increased mortality risk immediately after MI and is widely used as a risk stratification tool, it does not allow a distinction between those who will die of an arrhythmia and those who will die of other cardiovascular causes.4-8 Variable and unpredictable recovery of LV function after MI has consistently been noted immediately after an MI.5-7 Improvement in LVEF commonly begins within 3 days in patients who are revascularized with myocardial stunning and improved function of viable myocardium as the mechanisms.5-7 In the contemporary era of primary percutaneous coronary intervention for MI, of all revascularized patients with LVEF ≤40% at day 3, 24% will improve to have an LVEF ≥40% at 6 months.5-7 Other noninvasive and invasive risk stratification techniques used alone or in combination with the LVEF also lack sufficient predictive value for SCD in the immediate post-MI patient to have clinical utility for prevention of SCD.5-8

Despite many limitations, reduced LVEF remains the most powerful predictor of survival after an MI.4-8 When used to select patients remote from MI or revascularization, it identifies patients who derive a mortality benefit from the implantable cardioverter-defibrillator (ICD).5-12 Clinical trials assessing the ICD for primary prevention of SCD have demonstrated a reduction in sudden death and total mortality among patients with LV dysfunction caused by ischemic heart disease.5-12 These trials have excluded patients with recent MI or revascularization.5-12 Notably, the trials assessing the role of the ICD for SCD prevention immediately after MI have failed to show any survival benefit.13-15 Both the Immediate Risk Stratification Improves Survival (IRIS) trial and Defibrillation in Acute Myocardial Infarction Trial (DINAMIT) demonstrated a reduction in arrhythmic death that was offset by a significant increase in nonsudden death.13-15 This lack of benefit of the ICD in the immediate post-MI period may be due to the high frequency of cardiac rupture or recurrent MI relative to arrhythmic deaths.16 It logically follows that the benefit of the ICD in post-MI patients after 3 months may be due to a higher percentage of arrhythmic death than recurrent MI or cardiac rupture.16 Evidence-based medicine strongly supports contemporary guidelines restricting ICD implantations to patients at least 40 days after MI and 90 days after revascularization with continued impairment of LV function while on optimal medical therapy.17

In this issue of Circulation, Sjöblom and colleagues18 further investigate the time dependence of LVEF after MI and the implications for ICD eligibility. These investigators specifically evaluate the proportion of MI patients who improved their LV function by 3 months such that they would not qualify for an ICD implantation. Patients admitted for MI with reduced LVEF (≤40%) over a 3-year period to 2 hospitals were eligible for inclusion. Echocardiographic examinations were performed at the time of the diagnosis, at 5 days, and at 1 and 3 months after the MI. The main improvement in LVEF occurred by 1 month. The mean difference in LVEF over the next 2 months was small, 1.9%. During the first 9 weeks, 9 patients, representing 10% of the final cohort studied, suffered from life-threatening arrhythmias. Remarkably, all 9 patients survived cardiac arrest. Life-threatening arrhythmias occurred in 10% of the patients, illustrating the high risk for SCD in this population. Because there were no significant differences between the 9 patients who had cardiac arrest and those who did not, the investigators note that it is difficult to prevent SCD occurring shortly after an acute MI. The authors conclude that most patients improve their LVEF after acute MI and that in most patients the improvement could be confirmed after 1 month. They also note that these observations imply that further delay of ICD implantation may not be warranted.

Limitations acknowledged by the investigators include the subjective nature of the assessment of LVEF estimation resulting from a lack of proper visualization of the endocardium.18 The authors also note the potential for intraobserver...
and interobserver variations for calculating LVEF. A limitation not noted by the authors is the exclusion from the study of an unspecified number of patients with a life expectancy of <1 year or who declined informed consent. Of the 121 patients enrolled, 21 were excluded from analysis owing to disagreement of the LVEF estimation between the clinical echocardiography and the echocardiography core laboratory. Of the remaining 100 patients with an LVEF ≤40%, 9 patients dropped out of the study before hospital discharge. This includes 6 patients with severe heart failure, 1 patient with a cardiac embolus, and 1 patient with a pulmonary embolus.

Accordingly, of the 121 patients originally enrolled, only 91 patients were followed up after hospital discharge for the duration of the study.15 An indeterminate exclusion rate before enrollment and a subsequent dropout rate of 25% confound the interpretation of the outcomes. No additional information is provided on the 9 patients who dropped out of the study before hospital discharge. Only 2 of the 91 patients remaining in the study after hospital discharge died, both of infection, representing a 3-month total mortality of 2.2%.18 There were no arrhythmic deaths. Survival of all 9 patients having a cardiac arrest in the study contrasts with the survival rate averaging 10% of those receiving community-based resuscitation.1–3

On the basis of these exclusions and study dropouts, there is considerable potential for a selection bias favoring survival of those completing 3 months of follow-up. In this respect, the evolution and LVEF after acute MI and the implications for ICD eligibility presented by the investigators need to be carefully considered as potentially representing survival of other trials meeting the standards of evidence-based medicine, to guide early post-MI ICD implantation.20 Until this or a cardiac embolus, and 1 patient with a pulmonary embolus.

Although the observations by Sjöblom and colleagues18 extend prior observations on the time dependence of LVEF after MI, the small selected patient population, short follow-up, and absence of intervention limit the clinical utility of the observations. On the basis of prior interventional trials in high-risk patients immediately after MI, insufficient evidence still exists to support ICD implantation in those with impaired LVEF.15–17 Current guidelines restrict ICD implantations to patients at least 40 days after MI and 90 days after revascularization with continued impairment of LVEF while on guideline-based medical therapy.17 Unfortunately, the strategy of home automated external defibrillator use in high-risk patients immediately after MI has failed to improve survival compared with conventional resuscitation methods.19 Although the short-term use of noninvasive vent defibrillation represents a reasonable approach for high-risk post-MI patients on the basis of impaired LVEF, it has not been evaluated in prospective, randomized trials. Because neither noninvasive or invasive risk stratification techniques, alone or in combination with LVEF, have proven to have clinical utility, improved risk stratification tests and interventions are essential to reduce SCD and mortality after MI. Currently, a prospective, randomized trial is being conducted to investigate the role of cardiac magnetic resonance, with the ability to detect scar size and heterogeneity, in combination with programmed ventricular stimulation, to guide early post-MI ICD implantation.20 Until this or other trials meet the standards of evidence-based medicine by predicting and preventing SCD immediately after an MI, clinicians should focus on optimizing revascularization strategies and medical therapies. Clinical trials and current guidelines also support the reassessment of LVEF at least 40 days after MI and 90 days after revascularization to identify those with proven mortality benefit from ICD therapy.

Disclosures
Dr Estes reports educational consulting for Boston Scientific and St. Jude Medical and quality and safety consulting for Medtronic.

References


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