EDITORIAL COMMENT

Is Programmed Stimulation in Survivors of Myocardial Infarction Helpful?*

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Despite multiple advances in the early management of myocardial infarction (MI), late mortality among survivors of the acute episode remains a continuing problem. Numerous protocols have been proposed to "risk-stratify" MI survivors. Spontaneous and/or inducible ischemia and depressed left ventricular infarction are well-accepted markers for an adverse prognosis, and several strategies to treat ischemia and congestive failure have been shown to reduce mortality (1). A number of electrocardiographic and electrophysiologic risk factors for both sudden death and total mortality have also been characterized, including frequent or complex ventricular ectopy, baroreceptor sensitivity, heart rate variability, T-wave alternans, late potentials on a signal-averaged electrocardiogram (SAECG), and induction of ventricular tachycardia (VT) with programmed ventricular stimulation. Multiple observational studies have indicated that beta-adrenergic blocking drugs can improve mortality in MI survivors with one or more of these findings. However, until recently, studies with antiarrhythmic drugs have yielded either a negative effect (flecainide, encainide, mexiteline, d-sotalol), no net change ( dofetilide), or inconsistent benefit (amiodarone) (2). More recent studies of sudden death prophylaxis have focused on use of implantable cardioverter-defibrillators (ICDs) as tools to reduce sudden death and total mortality. Randomized trials, most notably the Antiarrhythmics Versus Implantable Defibrillators (AVID) trial (3), in patients who survived an episode of sustained VT or ventricular fibrillation have shown a significant decrease in mortality in the group receiving an ICD. Three published trials have evaluated ICD implantation for the primary, as opposed to secondary, prevention of sudden death. The Coronary Artery Bypass Graft (CABG) Patch Trial (4) found that ICD implantation did not improve survival among patients undergoing surgical coronary revascularization. The Multicenter Automatic Defibrillator Implantation Trial (MADIT) (5) enrolled patients with prior MI, a low left ventricular ejection fraction and spontaneous nonsustained and inducible sustained VT. The MADIT showed a highly significant reduction in total mortality among ICD recipients. Although the Multicenter Unsustained Tachycardia Trial (MUSTT) (6,7) was not specifically a trial of ICD therapy, the lowest mortalities in that trial were observed in those who eventually received an ICD.

CURRENT STUDY

In this issue of the Journal, Schmitt et al. (8) used programmed ventricular stimulation after MI to identify potential candidates for prophylactic ICD therapy. They screened a consecutive series of 1,436 MI survivors at a single hospital. During the acute phase, >90% of these patients underwent either a percutaneous coronary intervention or received thrombolytic therapy. In addition, >70% had a second revascularization procedure the second week after infarction. Thus, this population resembles the CABG Patch trial population in that almost all patients were aggressively revascularized. Patients also underwent a noninvasive risk-stratification protocol that included measurements of left ventricular ejection fraction, ventricular ectopy, heart rate variability, and an SAECG; >10 premature ventricular beats per hour or salvos of ventricular beats were the criteria used for significant ventricular ectopy. A risk score was then developed that assigned a value of 3 to subjects with a left ventricular ejection fraction of <40%, and values of 1 to those with ejection fractions between 40% and 49%, significant ventricular ectopy, abnormal heart rate variability, or late potentials on the SAECG. A total of 248 patients (17.6%) of the original group of 1,436 had a risk score of ≥3. Patients >75 years of age were excluded according to the study design. Of the remaining 194 patients, 98 (51%) underwent programmed ventricular stimulation using a standard protocol and criteria. Of these, 21 (22%) developed monomorphic VT in response to stimulation, and 20 of these 21 went on to receive an ICD. During follow-up (607 ± 424 days), 7 of these 21 patients with an ICD received therapy that was considered to be appropriate based on RR interval and stored electrogram analysis. Among the 77 patients who did not have inducible monomorphic VT, including 26 who had ventricular fibrillation, polymorphic VT, or VT with a cycle length of <230 ms, there was only one sudden death and no other arrhythmic events. Arrhythmic events, sudden death, or appropriate ICD therapy were more common in those with the lowest ejection fractions and risk scores of 4 or 5.

Despite the fact that over 1,400 patients were screened initially and the investigators’ careful follow-up of patients who did not undergo electrophysiologic study, any conclusions we draw from this study must be based on the event rates in the group of 98 patients who underwent programmed stimulation. The investigators found a 35% two-

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year occurrence of appropriate ICD therapy in the group with inducible VT compared with a 4% two-year sudden death rate in the group with negative or nonspecific responses to stimulation. These data should be compared with similar data from MADIT, MUSTT, and CABG Patch. In MADIT (5), the two-year mortality rate was 35% in the conventional therapy group, but more than half the deaths were not classified as sudden or arrhythmic. In MUSTT (6,7), the two-year cardiac arrest or arrhythmic death rate among those with inducible VT but off therapy was only 18%. The comparable rate in those without inducible VT was 12%. In CABG Patch (4,9), there was no difference in survival with ICD therapy, but a high proportion of the patients in the ICD group did receive ICD shocks. In that trial, however, most of the devices used did not have electrogram or RR interval storage, and it is thought that many of these shocks were for supraventricular arrhythmias. The use of an episode of ICD therapy, even when deemed appropriate based on stored electrogram review, is also problematic because device intervention in ICD recipients is more frequent than cardiac arrest or sudden death in comparable populations without an ICD (10). Although CABG Patch, MADIT, and MUSTT were conducted, for the most part, in patients without a very recent MI, the data from these three, much larger trials indicate that the current study by Schmitt et al. (8), because of the small number of patients in the final treatment group, may well overestimate the predictive value of the electrophysiologic study and the benefit of ICD treatment.

There is no disagreement that an ICD can terminate life-threatening ventricular arrhythmias. In many, but perhaps not all, populations, ICD therapy should prevent arrhythmic deaths and prolong overall lifespan. However, larger studies than the one here will be needed to permit accurate estimates of the clinical applicability, safety, and acceptance by patients and physicians of such an approach (11). In addition, studies on the cost-effectiveness of ICD therapy should include the cost of screening the initial population with whatever noninvasive and invasive tests that were used, as well as the cost of the device implant and follow-up. Prior economic analyses of ICD therapy have usually not included the potentially substantial costs of screening (12).

An alternate approach to that proposed by Schmitt et al. (8) would be to focus solely on an easily identified, high-risk group, those with the lowest ejection fractions. Even in the current study, patients with lower ejection fractions had the highest risk of receiving ICD therapy. In the European Myocardial Infarct Amiodarone Trial (EMIAT) (13), the event rate in the group with ejection fractions of ≤30% was over twice that in the group with ejection fractions between 30% and 40%. Several studies in which enrollment is based primarily on ejection fraction are now underway (14). Simply focusing on patients with the lowest ejection fraction would certainly be simpler and should be more attractive from a cost perspective than the multiple test strategy used in the Schmitt et al. (8) report.

**REFERENCES**


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