FRONTIERS IN CONGESTIVE HEART FAILURE
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Editor

Prophylactic Use of an Implantable Cardioverter-Defibrillator After Acute Myocardial Infarction

Abstract. *Background.* Implantable cardioverter-defibrillator (ICD) therapy has been shown to improve survival in patients with various heart conditions who are at high risk for ventricular arrhythmias. Whether benefit occurs in patients early after myocardial infarction is unknown.

Methods. We conducted the Defibrillator in Acute Myocardial Infarction Trial (DINAMIT), a randomized, open-label comparison of ICD therapy (in 332 patients) and no ICD therapy (in 342 patients) 6–40 days after myocardial infarction. We enrolled patients who had reduced left ventricular function (left ventricular ejection fraction, 0.35 or less) and impaired cardiac autonomic function (manifested as depressed heart-rate variability or an elevated average 24-hour heart rate on Holter monitoring). The primary outcome was mortality from any cause. Death from arrhythmia was a predefined secondary outcome.

Results. During a mean ($\pm$ SD) follow-up period of 30 ± 13 months, there was no difference in overall mortality between the two treatment groups: of the 120 patients who died, 62 were in the ICD group and 58 in the control group (hazard ratio for death in the ICD group, 1.08; 95% confidence interval [CI], 0.76–1.55; $p=0.66$). There were 12 deaths due to arrhythmia in the ICD group, as compared with 29 in the control group (hazard ratio in the ICD group, 0.42; 95% CI, 0.22–0.83; $p=0.009$). In contrast, there were 50 deaths from non-arrhythmic causes in the ICD group and 29 in the control group (hazard ratio in the ICD group, 1.75; 95% CI, 1.11–2.76; $p=0.02$).

Conclusions. Prophylactic ICD therapy does not reduce overall mortality in high-risk patients who have recently had a myocardial infarction. Although ICD therapy was associated with a reduction in the rate of death due to arrhythmia, that was offset by an increase in the rate of death from nonarrhythmic causes.— *Hohnloser SH, Kuck KH, Dorian P, et al. Prophylactic use of an implantable cardioverter-defibrillator after acute myocardial infarction.* N Engl J Med. 2004;351:2481–2488.

Comment. We review the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) below, so it is timely to review another important trial: the DINAMIT—the first randomized controlled study to assess the impact of implantable cardioverter-defibrillator (ICD therapy very early after myocardial infarction (MI). DINAMIT was designed to test whether prophylactic implantation of an ICD would reduce mortality in survivors of a recent MI who are at high risk for ventricular arrhythmias. Patients aged 18–80 years were enrolled if they recently had an MI (6–40 days previously) and if they had a left ventricular ejection fraction of 35% or less. This trial randomized 674 patients within 40 days of an acute MI to current standard medical therapy with or without an ICD and followed them for a mean of 2.5 years. Three hundred thirty-two patients were randomly assigned to the ICD group and 342 to the control group. The mean left ventricular ejection fraction was 28%. The average time from MI to randomization was 18 days and was similar in the two groups. There was excellent adherence to optimal medical therapy in both groups, which included angiotensin-converting enzyme inhibitors, β blockers, aspirin, and lipid-lowering drugs. Patients who were randomly assigned to receive an ICD were required to undergo implantation of a market-approved, single-chamber ICD (St. Jude Medical, Sunnyvale, CA) within 1 week after randomization. The primary outcome in DINAMIT was death from any cause. Death due to cardiac arrhythmia was the secondary outcome. There was no difference in overall mortality between the two groups. Of the 120 who died, 62 were in the ICD group and 58 in the control group (hazard ratio for death in the ICD group, 1.08; $p=0.66$). There were

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12 deaths due to arrhythmia in the ICD group compared with 29 among controls (hazard ratio for the ICD group, 0.42; $p=0.009$). In contrast, there were 50 deaths from nonarrhythmic causes in the ICD group, but only 29 in the controls (hazard ratio for the ICD group, 1.75; $p=0.02$). In essence, in DINAMIT, the reduction in the rate of arrhythmia-related death was very similar to that observed in previous trials of ICD therapy.

In contrast to the previous trials, however, DINAMIT revealed a statistically significant increase in the rate of death from nonarrhythmic causes among patients assigned to receive an ICD. Most of these deaths (78%) were cardiovascular in nature. It appears that in DINAMIT, as in previous trials of ICD therapy, the ICD prevented death from ventricular fibrillation; however, preventing death from ventricular fibrillation did not reduce overall mortality in these patients. The reason for the unexpected and unprecedented increase in mortality from causes other than arrhythmia in patients assigned to receive an ICD is not clear. There was no sign of an increased rate of death in association with the surgical procedure or complications with the use of the ICD. It is unlikely that the increased rate of deaths from cardiac, nonarrhythmic causes was due to excessive pacing because the backup pacing was programmed at a very low rate in almost all the patients in the ICD group. Regardless of the plausible mechanism, this important clinical trial identifies a group of patients with risk factors for sudden death from cardiac causes in whom ICD therapy may not provide a survival benefit.

DINAMIT suggests that patients with a recent MI and acute-onset left ventricular systolic dysfunction (left ventricular ejection fraction even less than 35%) do not benefit from ICDs for overall survival. One should wait until everything is stabilized following an MI—a period of perhaps 6 weeks—before prophylactic implantation of an ICD is considered.

Amiodarone or an Implantable Cardioverter-Defibrillator for Congestive Heart Failure

Abstract. *Background.* Sudden death from cardiac causes remains a leading cause of death among patients with congestive heart failure (CHF). Treatment with amiodarone or an implantable cardioverter-defibrillator (ICD) has been proposed to improve the prognosis in such patients.

Methods. We randomly assigned 2521 patients with New York Heart Association (NYHA) class II or III CHF and a left ventricular ejection fraction (LVEF) of 35% or less to conventional therapy for CHF plus placebo (847 patients), conventional therapy plus amiodarone (845 patients), or conventional therapy plus a conservatively programmed, shock-only, single-lead ICD (829 patients). Placebo and amiodarone were administered in a double-blind fashion. The primary end point was death from any cause.

Results. The median LVEF in patients was 25%. Seventy percent were in NYHA class II, and 30% were in class III CHF. The cause of CHF was ischemic in 52% and nonischemic in 48%. The median follow-up was 45.5 months. There were 244 deaths (29%) in the placebo group, 240 (28%) in the amiodarone group, and 182 (22%) in the ICD group. As compared with placebo, amiodarone was associated with a similar risk of death (hazard ratio, 1.06; 97.5% confidence interval [CI], 0.86–1.30; $p=0.53$) and ICD therapy was associated with a decreased risk of death of 23% (hazard ratio, 0.77; 97.5% CI, 0.62–0.96; $p=0.007$) and an absolute decrease in mortality of 7.2 percentage points after 5 years in the overall population. Results did not vary according to either ischemic or nonischemic causes of CHF, but they did vary according to the NYHA class.

Conclusions. In patients with NYHA class II or III CHF and LVEF of 35% or less, amiodarone has no favorable effect on survival, whereas single-lead, shock-only ICD therapy reduces overall mortality by 23%.—*Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure.* N Engl J Med. 2005;352:225–237.

Comment. This trial was initially presented at the American College of Cardiology 2004 Scientific Sessions but was published only recently. It is one of the major trials which will define the future of heart failure (HF) therapy. The trial randomized 2521 patients with New York Heart Association class II or III CHF and LVEF ≤35% to receive a single-lead ventricular ICD programmed to shock-only mode or either amiodarone or a matching placebo, with the latter two arms conducted double blind. It is worth noting that this trial recruited both ischemic and nonischemic HF patients. All patients were on "state-of-the-art background medical therapy" for HF that overwhelmingly included β blockers and either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. Patients assigned to amiodarone or matching placebo began therapy as outpatients immediately after randomization. Patients assigned to ICD therapy received their device over a median of 3 days after randomization. At baseline, the median LVEF of patients was 25%; 70% had New York Heart Association class II HF, and 30% had class III HF. The median follow-up for all surviving patients was 45.5 months. All surviving patients were followed for at least 2 years. The primary end point of the trial was death from any cause. A total of 666 patients died: 244 (29%) in the placebo group; 240 (28%) in the amiodarone

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group; and 182 (22%) in the ICD group. As compared with placebo, amiodarone therapy was associated with a similar risk of death (hazard ratio, 1.06; 97.5% CI, 0.86–1.30; $p=0.53$) and ICD therapy was associated with a decreased risk of death (hazard ratio, 0.77; 97.5% CI, 0.62–0.96; $p=0.007$). The significant ICD survival benefit was independent of whether HF was ischemic or nonischemic in origin.

The authors deduced two principal findings. First, therapy with a conservatively programmed, shock-only ICD significantly decreased the relative risk of death by 23%, resulting in an absolute reduction of 7.2 percentage points at 5 years among patients with HF who received state-of-the-art background medical therapy, and the benefit did not vary according to the cause of HF. Second, amiodarone had no beneficial effect on survival, despite the use of appropriate dosage and reasonable compliance rates over longer periods than in other placebo-controlled trials. In this trial, single-lead ICDs had a 5% rate of acute device-related complications and a 9% rate of chronic complications.

Overall, this is a great trial which was well done. It is very important to emphasize, however, that this trial deals with patients who had chronic HF and were treated well with current standard medical therapy for HF. Patients presenting for the first time with HF and a low LVEF should not receive ICDs before being treated with standard HF medical therapy. So, in essence, physicians should achieve maximal medical management before proceeding with ICD.

In patients with New York Heart Association class II or III HF and LVEF of 35% or less, amiodarone has no favorable effect on survival. In contrast, shock-only ICD therapy improves survival beyond the improvement afforded by the current standard HF therapy. On a population basis, we will save one life for every 14 patients treated with ICD for 5 years.