Mortality Risk and Defibrillator Benefit After Myocardial Infarction

To the Editor:

In their article, Wilber et al1 showed that an implantable defibrillator (ICD) provided a substantial reduction in mortality for patients with remote myocardial infarction (MI), but almost no survival benefit was found in patients with recent MI (<18 months). They concluded a time dependence of ICD benefit and hypothesized that the survival benefit in patients with recent MI would become greater if follow-up was extended longer.

In our opinion, another hypothesis has to be considered when analyzing the reported data and, also, because of the major implications it might have. If, as the authors suggested, survival benefit of ICD would be greater by extending follow-up longer, we would expect an increasing benefit for the last three quartiles as time from most recent MI to enrollment increases. In contrast, the hazard ratios for the effect of ICD for the quartiles 18 to 59, 60 to 119, and ≥120 months do not show an increasing survival benefit as time from MI increases but, rather, a trend toward a decreasing benefit (0.52 to 0.62). Because the arrhythmic death risk does not seem to increase as a function of time, other hypotheses have to be considered to explain the lower risk of sudden death in patients with recent MI.

In view of the evolution in management of acute MI over the last 15 years, patients with recent MI not only differ from those with remote MI with regard to time from MI (and baseline characteristics), but also from the treatment received in the acute and subacute phase of MI. Patency of the infarct-related artery achieved by early and late (>24 hours after MI) reperfusion reduces arrhythmic mortality independent of left ventricular (LV) function preservation.2,3 As a result, the increasing implementation of early reperfusion and a more systematic coronary angiography evaluation of patients with LV dysfunction in the subacute period (with late reperfusion) may explain the lower risk of arrhythmic death despite similar ejection fraction in patients with recent MI. Modern drug therapy instituted early in the course of MI, as for the prevention of ventricular remodeling, may also explain a lower subsequent arrhythmic risk.

The authors raised the question of whether it would be appropriate to defer implantation of ICD. Awaiting the follow-up to be extended, the question should rather be whether patients with reduced LV function and MI sustained in 2004 still deserve a prophylactic defibrillator without additional risk stratification.

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Response

Drs Pascale, Kappenberger, and Frommer raise several important issues regarding our further analysis of the Multicenter Automatic Defibrillator Implantation Trial (MADIT) II database.1 The major findings were that mortality risk increased as a function of time from myocardial infarction (MI) and that the survival benefit with implantable defibrillator (ICD) therapy remained significant for up to 15 years. The hazard ratios for ICD therapy in the 3 remote time quartiles were virtually the same (0.52, 0.50, and 0.62, respectively) as that for recent MI (<18 months), suggesting little benefit (0.98). We concluded that ICD implantation in patients with left ventricular ejection fraction (LVEF) ≤30% should be strongly considered even several years after MI, not that it should be withheld in patients after recent MI.

There are multiple potential reasons for the trend toward lesser ICD benefit early post-MI, and these include the possibility of chance. Pascal and coauthors suggest that contemporary therapy (early reperfusion and exposure to β-blockers and angiotensin-converting enzyme inhibitors) has altered the biology of “modern” infarcts to render them more electrically stable relative to MI incurred 10 to 15 years ago when such therapies were less widely used. However, despite substantial reductions in the proportion of post-MI patients with severely reduced LVEF after these early interventions, those with LVEF ≤30% continue to have considerably higher long-term mortality.1,2 We agree that these issues require additional study.

Deferral of prophylactic ICD implantation in the very early phase of MI (<1 month, excluded in MADIT II) may be appropriate. Many patients undergo significant alterations in ventricular function within this time period, and the initial LVEF may be a poor marker of long-term risk.2 Instructive in this regard are the preliminary results of the Defibrillator in Acute Myocardial Infarction Trial (Connolly SJ, Hohnloser SH. Late breaking clinical trials: DINAMIT. Presented at the American College of Cardiology Scientific Sessions, 2004), which demonstrated a ≈15% mortality at 2 years in both ICD and control patients enrolled <40 days after MI. This mortality is lower than that observed in the MADIT II cohort (16% ICD-treated, 22% control).

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