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Reply to the Editor-- When to implant an ICD following a Myocardial Infarction?

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Barra et al. astutely point out that if one were to examine the treatment effect of the implantable cardioverter-defibrillator (ICD) during the first year after myocardial infarction (MI) in its entirety rather than parsing the same data into two smaller subgroups in our study,[1]the overall treatment effect of the ICD would be reduced in comparison to other time periods on the basis of hazard ratio point estimates. They report that these findings are consistent with those of the Multicenter Automated Defibrillator Implantation Trial II (MADIT-II)[2] and the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT),[3] where the benefit of the ICD emerged after 2–5 years of follow-up. The follow-up of MADIT-II and SCD-HeFT has been reported to 8 years[4] and 5 years,[3] respectively. Close examination of the survival curves comparing ICD recipients to non-recipients reveals that the groups began to separate in the first few months in MADIT-II and approximately 18 months in SCD-HeFT. However, a statistically significant difference between groups was not reached until later when enough events had accumulated. This latency is an artifact of sample size and corresponding power rather than an absence of ICD benefit. Sample size limitation in fact served as the impetus for the pooling of trial data and the current analysis in which an interaction between time from MI and all-cause mortality was not observed.

Barra et al. also recognize that patients with multiple comorbidities are underrepresented in clinical trials. Citing a secondary analysis of MADIT-II,[5] they suggest that patients on either end of the spectrum of health—the extremely hale or the exceptionally ill—may not benefit from ICDs. The absence of benefit observed among these patients may reflect a shortcoming of subgroup analysis. With few patients and in turn events, conclusions are speculative. Another analysis of pooled trial data to address this question may yield important insights. Until further data become available, we do not support waiting a year after MI in Darwinian fashion to ascertain the degree of comorbidity. Rather, we favor the careful exercise of clinical judgment when assessing a patient's comorbidities and in turn prognosis before recommending an ICD. Extrapolating from the current analysis, we do not advocate taking into account time from MI outside of 40 days.

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Barra et al. also question whether the role of an electrophysiology study in enrollment and randomization in MADIT-I and MUSTT can explain the observed benefit of ICD placement in these studies 41–180 days after MI relative to other trials. In MADIT-II, however, noninducible patients had substantial ventricular tachycardia and more ventricular fibrillation than inducible patients.[6] Further, our statistical model took into account inter-trial variation of treatment effects and parameters associated with trial-specific baseline hazards of death by assuming random effects. In view of this statistical model, we believe the impact of the electrophysiology study on our estimation of ICD treatment effects is negligible.

Finally, Barra et al. muse whether ICD programming according to MADIT-Reduce Inappropriate Therapy (RIT)[7] criteria would improve survival in the first year after MI. Given the small number of deaths in the trial overall, subgroup analysis was limited. A potential mechanism underlying an interaction between device programming efficacy and time from MI would be complex. Pending further data, we advocate MADIT-RIT programming for primary prevention ICD recipients irrespective of the time from most recent MI.

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