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Letter to the Editor— When to implant an ICD following a myocardial infarction?

Hess et al[1] conclude that there does not seem to be any evidence suggesting that the efficacy of primary prevention implantable cardioverter-defibrillator (ICD) therapy depends on time to implantation >40 days after myocardial infarction (MI). Their findings were based on the results of 4 primary prevention ICD trials—Multicenter Automatic Defibrillator Implantation Trial (MADIT-I), Multicenter Unsustained Tachycardia Trial (MUSTT), MADIT-II, and Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT)—and may support our current understanding of who is the best candidate for an ICD.

Although a previous post hoc analysis of the SCD-HeFT trial shared the same results,[2] our interpretation of the present meta-analysis data is slightly different. In fact, hazard ratios obtained using the adjusted Bayesian Weibull survival model indicate a potential interaction between time from MI and all-cause mortality, as those implanted with an ICD 1–5 years after MI seemed to fare better. This is in accord with data from MADIT-II and SCD-HeFT, in which benefit of the ICD in the primary prevention of sudden cardiac death emerged only in a mid- to long-term follow-up (2–5 years).[3]

Randomized controlled trials are not usually representative of the whole population as they tend to exclude patients deemed to have a poorer prognosis. For example, MADIT-II excluded "all patients with any condition other than cardiac disease that could associate with high likelihood of death during the trial." Furthermore, patients with higher comorbidity burden tend to be unconsciously excluded even when fulfilling inclusion criteria. These patients are at higher arrhythmic and especially nonarrhythmic mortality risk and probably do not get the same survival benefit from an ICD compared to their "healthier" counterparts. For example, in a post hoc subanalysis of patients from MADIT-II, there was no difference in the 2-year mortality rates for patients with an estimated glomerular filtration rate <35 mL/(min $\cdot$ 1.73 m^2) randomized to an ICD or conventional treatment.[4] Natural selection implies that those surviving the first year after MI are at a relatively lower nonarrhythmic mortality risk and may have a lower comorbidity burden and thus a longer life expectancy; therefore, they could potentially benefit from an ICD. Hence, in addition to the current controversy regarding the potential benefit, or lack thereof, of an ICD in patients with multiple markers of organ dysfunction,[5] the best timing for its implantation in this cohort remains mostly unknown. We speculate that in the range of patients covered by the guidelines, the *healthier* the patients the more likely they are to either get no benefit from an ICD or need several years to start benefiting. A study by Goldenberg et al[6] seems to support this thesis, as patients without risk factors such as New York Heart Association class higher than II, age >70 years, urea level >26 mg/dL, QRS duration >120 ms, and atrial fibrillation did not get any benefit from the ICD. On the contrary, supposedly *sicker* individuals (eg, those with multiorgan dysfunction) are not expected to get much benefit in the first year after MI, as they tend to die from nonarrhythmic causes but may eventually be good candidates if they survive the first year.

Patients from MADIT-I and MUSTT were the ones benefiting the most from an ICD implantation in the first 6 months, which may suggest that the electrophysiological study might be useful for identifying those entitled to an early ICD, although routine performance of an electrophysiological study in these patients is not currently recommended.

Finally, we wonder whether an ICD programming in the 4 trials similar to that of the MADIT-Reduce Inappropriate Therapy study could potentially improve overall survival, decrease the high incidence of inappropriate shocks, and allow a benefit of the ICD in the first year after MI.

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