

## **Long-Term Outcome after Implantation of a Cardioverter Defibrillator: An Eight Year Follow-Up Study of the Multicenter Automatic Defibrillator Trial II**

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**Room:** Ballroom West

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**Background:** The Multicenter Automatic Defibrillator Trial II (MADIT-II) showed a significant reduction in the risk of death with an implantable cardioverter defibrillator (ICD) during a mean follow-up period of 20 months. However, the long-term benefit defibrillator implantation is unknown.

**Methods:** MADIT-II enrolled 1232 patients with ischemic left ventricular dysfunction who were followed up through November 2001. For the current long-term efficacy study we acquired post-trial mortality data from the U.S. (through December 2006) and European (through March 2009) National Death Registries. Multivariate Cox proportional hazards modeling was carried out to assess the long-term outcome of ICD vs. non-ICD treated patients. Data regarding crossover between treatment arms, obtained 2 months after trial closure, were assessed using time-dependent analysis and further validated by censoring follow-up at the time of change in treatment arm. Survival analysis was assessed using a modification of the Kaplan-Meier method, allowing non-ICD to ICD crossover.

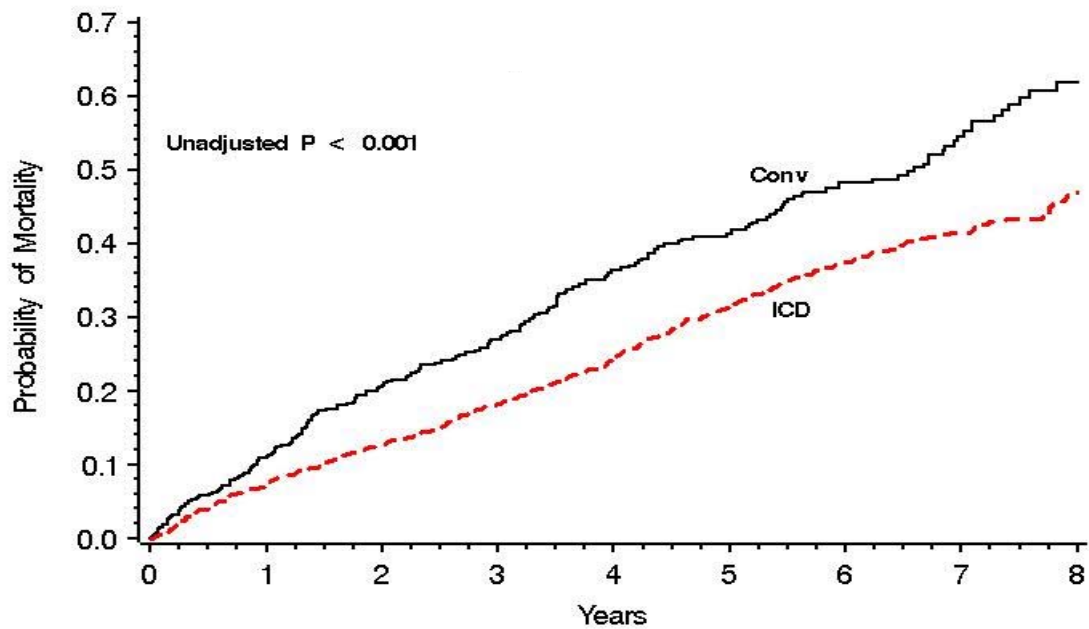
**Results:** At 8 years of follow-up, the cumulative probability of all-cause mortality was 45% among patients treated with an ICD as compared with 61% among patients without an ICD ( $p < 0.001$ ; Figure 1), corresponding to 1.2 life-years saved with an ICD during the 8-year period. Multivariate analysis demonstrated that ICD therapy was associated with improved survival throughout the 8-year follow-up ( $HR = 0.63$ ;  $p < 0.001$ ). When outcome was assessed separately during the early and late phases of the follow-up period, ICD therapy was shown to be associated with a significant survival benefit during the first 4 years after enrollment ( $HR = 0.59$ ;  $p < 0.001$ ); and with additional life-saving benefit during the extended 4-8 year follow-up period ( $HR = 0.71$ ;  $p = 0.02$ ).

Post-trial ICD efficacy was shown to be influenced by heart failure (HF) status at trial closure: patients who did not experience symptomatic HF during the trial derived a pronounced survival benefit from the ICD after trial closure ( $HR = 0.52$ ;  $p = 0.002$ ), whereas post-trial ICD efficacy was significantly attenuated among patients who developed symptomatic HF during the study ( $HR = 0.87$ ;  $p = 0.34$ ;  $p$ -value for ICD x HF interaction = 0.04). Furthermore, device-pacing programming was shown to affect long-term outcome with an ICD: patients who received dual-chamber devices during the trial (set to pacing rate at DDD-60 to 70) experienced an increase in mortality rate during the late phase of the extended follow-up period (Figure 2), and accordingly did not derive a significant benefit from the ICD during the post-trial period ( $HR = 0.88$ ;  $p = 0.35$ ), whereas patients who received single-chamber devices (set to back-up pacing rate at VVI-40 to 50) derived enhanced benefit from the ICD during the post-trial period ( $HR = 0.70$ ;  $p = 0.009$ ).

**Conclusions:** In MADIT-II, the survival benefit from the ICD was sustained over 8 years of follow-up. Long-term device efficacy was enhanced among patients who received a limited amount of right ventricular pacing from the ICD, and among those who did not develop HF progression during the study.

[Figures 1 and 2 on the following page]

**Figure 1**



**Figure 2**

