

## MADIT II prematurely terminated: Major impact on health economics?

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Last November the independent Data and Safety Monitoring Board (DSMB) of the MADIT II trial decided to prematurely terminate the study because a significant improvement in survival had been found in the group of patients receiving an implantable cardioverter defibrillator (ICD). The MADIT II trial followed an earlier study (MADIT) that already had demonstrated that ICD has a significant benefit in patients with past myocardial infarction, low ejection fraction, spontaneous non-sustained ventricular tachycardia, and non-suppressible inducible sustained ventricular tachycardia during electrophysiologic study. The MADIT II trial addressed a potentially much larger patient population because the inclusion criteria were extremely simple: previous myocardial infarction (more than one month before inclusion) and a left ventricular ejection fraction of 30% or less. More than 1200 patients were included in the study, which was carried out at 71 United States and 5 European centers. Patients were randomized to receive an ICD or not. No antiarrhythmic drugs were given in this trial. Patients were followed-up for an average time of about 2 years. The DSMB prematurely terminated the trial after analysis showed a reduction in mortality of about 30% in the ICD group compared to the non-ICD group. Definitive data will be reported soon by the investigative team.

**What are the implications of MADIT II? Will it really have an impact on prophylactic implantation of ICDs? Will it drive policy makers to revise the indications for ICD implantation? My guess is not. Let me try to explain you why**

Before MADIT II, the MADIT, MUSTT and AVID trials had already demonstrated the greater or lesser benefit of ICD as compared to conventional an-

tiarrhythmic drug treatments. To some extent, the trials confirmed what rhythmologists already knew in practice, that the major determinant of prognosis in patients with coronary heart disease who have suffered a myocardial infarction is the degree of left ventricular damage. As rhythmologists we have always taken care of the post myocardial infarction population with the greatest impairment: the population with severe left ventricular damage, the one prone to developing any possible complications, including heart failure and, of course, sudden arrhythmic death.

Initially, rhythmologists dealt with the problem of arrhythmias in a somewhat retrospective way: Arrhythmias were treated only after the patient had presented one or more episodes of spontaneous sustained ventricular arrhythmias. The means to treat arrhythmias were limited to antiarrhythmic drugs. As most patients did not survive the first cardiac arrest (because they were too sick to survive), the impression gained was that antiarrhythmic drugs were helpful. But that was just a bias because the survivors were the least affected of a very ill group of patients. The first conceptual shock came when antiarrhythmic drugs were used prophylactically, as in the CAST study. Whatever the design and population included, CAST really started a new era in antiarrhythmic treatment and these drugs were never again looked at in the same way.

The potential pro-arrhythmia effects of these drugs, rather than their possible benefits, became the center of attention. The door opened wide for trials testing the hypothesis that the ICD was better than antiarrhythmic drugs or nothing. And while the criteria for inclusion in these different studies varied, they all included the major risk factor, poor left ventricular function.

After the results of the MADIT and MUSTT trials were reported, it was predicted that they would have a major impact on the ICD implantation rate. In practice, that was not the case and the reasons for this are simple: 1) The potential population meeting the inclusion criteria is decreasing because of more aggressive treatment of myocardial infarction during the acute

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phase, and 2) The type of patients included in the studies were already being implanted. In the short term, MADIT and MUSTT confirmed that patients with a poor prognosis required implantation of an ICD. In the long term, implantation rates in developed countries did not change too much. MADIT II addresses a patient population for which the prophylactic implantation of an ICD is already accepted in many countries, including Belgium. The results of MADIT II are most welcome as they confirm what rhythmologists knew: the sicker you are, the worse you do. For the very ill patient, any help is welcome. MADIT II confirms that the ICD is better than nothing

for the survivor of a myocardial infarction that has been poorly prevented and treated, resulting in severe myocardial damage. Future efforts should continue to be directed toward preventing acute occlusion of a coronary artery and treat such occlusions appropriately if they occur, thereby avoiding their nasty consequences. I do not predict any dramatic consequences of MADIT II for the already shrinking European health care budgets. But irrespective of the MADIT II trial, choices in health care expenditures will soon have to be made. Do we want to pay for an ICD for someone who continues to smoke in spite of having many risk factors? To be continued.