More good news on prophylactic arrhythmia management

Implantable cardioverter-defibrillators are clearly beneficial in patients who have suffered aborted sudden cardiac death or symptomatic and sustained ventricular tachycardia in the presence of impaired left ventricular dysfunction. For this patient cohort, implantable cardioverter-defibrillator implantation is now the treatment of first choice and unequivocally superior to antiarrhythmic drug treatment, as has been shown in AVID\[1\], CIDS\[2\] and CASH\[3\].

The role of implantable cardioverters in primary prevention of arrhythmic death has been much more controversial. It is well known that patients with non-sustained ventricular tachycardia, in the presence of coronary artery disease and especially after myocardial infarction, are at higher risk of sudden death. Until recently, however, it was unclear whether antiarrhythmic therapy provides any benefit. Some trials studying antiarrhythmic agents in post-myocardial infarction patients have even shown an increased mortality. The role of arrhythmia treatment, however, became clearer when the results of MADIT\[4\] (Multicenter Automated Defibrillator Trial) were announced at the NASPE meeting in May 1996. This trial, the results of which were eventually published at the end of 1996, included patients with coronary artery disease and depressed left ventricular function remote from myocardial infarction. These patients presented with asymptomatic (or only mildly symptomatic) non-sustained ventricular tachycardia with a mean length of nine beats. Patients were randomized to implantable cardioverter-defibrillator therapy or conventional treatment if a ventricular tachycardia was inducible during electrophysiological study and could not be suppressed by procainamide. MADIT was the first randomized study to demonstrate a benefit from implantable cardioverter-defibrillator implantation. In fact, it showed a more than 50% reduction in total mortality in the implantable cardioverter-defibrillator group.

In the meantime, the inclusion criteria for MADIT is now a Class I ACC/AHA implantable cardioverter-defibrillator indication\[5\]. However, MADIT was heavily criticized for several points, among them an imbalance in the beta-blocker treatment in favour of the implantable cardioverter-defibrillator group. For this reason, and because other trials failed to show a benefit from prophylactic implantable cardioverter-defibrillator implantation, the results of MADIT have not readily been adopted into everyday clinical practice and MADIT has led only to a very modest increase in implantable cardioverter-defibrillator implants.

At the last meeting of the American College of Cardiology (ACC), Dr Alfred Buxton from the Temple University School of Medicine in Philadelphia, U.S.A. presented the results of the MUSTT trial (Multicenter Unsustained Tachycardia Trial) which was conducted in the United States and Canada\[6\]. MUSTT was not designed to test implantable cardioverter-defibrillator therapy vs drug therapy but to determine whether antiarrhythmic therapy, guided by electrophysiology, can decrease the risk of arrhythmic death and cardiac arrest in patients with non-sustained ventricular tachycardia, left ventricular dysfunction (ejection fraction <40%), and coronary artery disease. The patients included in MUSTT were similar to MADIT patients, but presented with markedly shorter runs of non-sustained ventricular tachycardia. About 35% of the enrolled 2202 patients had inducible ventricular tachycardia. Of these, 704 were randomized to conservative

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treatment (including beta-blockers and/or ACE inhibitors) or electrophysiology-guided treatment including implantable cardioverter-defibrillator implantation for patients who were refractory to at least one antiarrhythmic agent (propafenone or sotalol could be used in the first round of treatment). The primary end-points in this study were arrhythmic death or cardiac arrest.

In the antiarrhythmic therapy group, 45% of patients received antiarrhythmic drugs and 46% received an implantable cardioverter-defibrillator. During the follow-up of more than 3 years, the antiarrhythmic therapy group performed significantly better than the conservative group (arrhythmic mortality at 2 and 5 years of 12% and 25% vs 18% and 32%, respectively, \( P = 0.043 \)). Most important was the subgroup analysis, revealing that the patients who received an implantable cardioverter-defibrillator clearly performed better than any other group, with 92% being alive at 60 months. In fact, when the implantable cardioverter-defibrillator patients were removed from the antiarrhythmic therapy group, there was no significant difference between the conservative group and the antiarrhythmic drug group.

Thus, MUSTT, which intended to investigate treatment strategies (conservative treatment vs electrophysiology-guided antiarrhythmic treatment) rather than to compare various forms of antiarrhythmic treatment impressively confirmed the results of MADIT.

**Clinical implications**

The available data demonstrate the superiority of implantable cardioverter-defibrillator therapy over currently available antiarrhythmic drugs under several clinical conditions: after a documented severe arrhythmic event and as a prophylaxis. MADIT and MUSTT showed that prophylactic implantable cardioverter-defibrillator implantation is life-saving for patients with non-sustained ventricular tachycardia, impaired left ventricular function and coronary artery disease, who have inducible ventricular tachycardia. It should be emphasized again, that the patients included into these studies were asymptomatic, thus necessitating the screening of the post-myocardial infarction population if these patients are to be saved from arrhythmic death. Thus, these results have major implications for our management of patients with severe ventricular tachyarrhythmias. The need for health-care resources is substantial and may become a major limiting factor in many countries. The expansion in the use of implantable cardioverter-defibrillators should lead to markedly reduced device prices, especially if less sophisticated devices were used in patients who might do well with a shock-only device. Upgrading such a device later on, when recurrent monomorphic ventricular tachycardia should supervene instead of ventricular flutter or fibrillation, might be one solution.

With increasing knowledge about arrhythmogenesis, new moves need to be discussed including a broader, multidimensional approach. These should include treatment or reversal of arrhythmia conditioning, and triggering factors, as well as suppression of the arrhythmia directly, possibly by new antiarrhythmic agents. Given the proven efficacy of implantable cardioverter-defibrillators, however, novel antiarrhythmic agents and strategies need to be developed under the safety net of an implanted defibrillator.

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**References**


