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Editorial

Update of the guidelines on sudden cardiac death of the European Society of Cardiology

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One of the most important challenges for scientific societies responsible for the development of guidelines, is to provide regular update of recommendations when new data become available. The Committee for Practice Guidelines of the ESC has set the goal of producing an update of guidelines every 12–24 months from the publication of the initial document (http://www.escardio.org).

The guidelines for the prevention of sudden cardiac death (SCD) were published in the August issue of the European Heart Journal in 2001[1] and the Executive Summary was published in the January issue of Europace.[2] In the last 12 months, the release of important data has affected risk stratification and management of patients at risk of dying suddenly. Based on this evidence, the members of the Task Force on SCD of the ESC have decided to revise the original document. The updated version of the full document will be published on the ESC website. Here, we review the evidence that has led to the update of two sections: (1) primary prevention of SCD in post-myocardial infarction (MI) and heart failure, and (2) primary prevention of SCD in dilated cardiomyopathy (DCM).

Primary prevention of SCD in post-MI and heart failure

The revision of the section of primary prevention of SCD in post-MI and heart failure has been considered appropriate based on the release of the results of the Multicenter Automatic Defibrillator Implantation Trial II (MADIT II) trial.[3] This study was designed to investigate whether the implantable cardioverter defibrillator (ICD) would be effective in the prevention of all-cause death in patients with post-MI and low (≤30%) ejection fraction (EF). The study was based on the assumption that ICD would reduce all-cause death by 38% at 2-years with a 95% power and a probability value of 0.05. A randomization ratio of 3:2 to receive either an ICD or conventional medical therapy was selected. Analysis of primary endpoint was performed using a triangular sequential design, similar to the one adopted in the MADIT trial.[4]

After inclusion of 1232 patients, the MADIT II study was terminated because of a significant (31%) reduction in all-cause death in patients assigned to ICD therapy.

MADIT II provides evidence that patients meeting the study entry criteria have a better survival if they receive a prophylactic ICD. The benefit was reflected in a 12, 28 and 28% death reduction at years 1, 2 and 3 of follow-up, respectively. Notably, the incidence of heart failure was higher (19.9%) in patients assigned to ICD than in patients receiving conventional therapy only (14.9%).

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Table 1 Primary prevention in post MI with or without HF

	Class I	Class IIa	Class IIb
Post-MI	Beta blockers ACE inhibitors Aspirin Lipid lowering drugs	PUFA Amiodarone	
MI+ LV dysfunction	Beta blockers ACE inhibitors Aldosterone receptor blockers	Amiodarone ICD (if EF≤30%)	
Hemodynamically tolerated VTs		Amiodarone Beta blockers	ICD Ablation Surgery
EF≤40%+spont. VTns+VTs inducible at PES	ICD		

MI—myocardial infarction; ACE—angiotensin converting enzyme; LV—left ventricular; VTns—non sustained ventricular tachycardia; VTs—sustained ventricular tachycardia; PUFA—polyunsaturated fatty acids; ICD—implantable cardioverter defibrillator; EF—ejection fraction

Results of MADIT II suggest that ICD therapy may be indicated for primary prevention of all-cause death in patients post-MI with an EF≤30%.

The members of the Task Force have carefully discussed how to incorporate the results of the present study in the recommendations for the use of the ICD in primary prevention of SCD in patients after MI and left ventricular dysfunction. The committee has agreed that, before a Class I recommendation is provided for ICD in post-MI patients with EF≤30%, it would be important that concordant results are obtained in at least another study addressing the same issue. The concern has been raised that early termination of the trial as a result of the triangular sequential design may have led to an overestimate of the long-term benefit of ICD therapy. It has also been argued that MADIT II does not include an antiarrhythmic drug arm. Specifically, amiodarone was not investigated based on negative findings obtained in previous trials in patients with congestive heart failure. However, it should be acknowledged that the population of patients in those earlier studies was different from that of the MADIT II as outlined by a rate of 70% of patients in NYHA class I or II in this latter trial. More information on the role of amiodarone is expected from an ongoing trial, the SCD-Heft, in which, however, entry criteria are substantially different from those used in the MADIT II.

Furthermore, since Holter recording was not performed in MADIT II, patients meeting MADIT[4] criteria (i.e. spontaneous occurrence of non-sustained ventricular tachycardia (VTns) and inducible/non-suppressible ventricular tachycardia (VT) during programmed electrical stimulation) were not excluded from enrollment—the contribution of this subgroup of patients to the results of MADIT II therefore remains unclear.

Furthermore, secondary endpoint analyses of MADIT II are ongoing: it is expected that they will provide data on the value of additional risk stratification parameters in this population of patients. Similarly, MADIT II investigators are expected to present data on the expected prolongation of life and the cost per 'year of life saved' of ICD in the MADIT II population.

In summary, based on these considerations a recommendation for a Class IIa with a level of evidence B has been issued (Table 1).

Primary prevention of SCD in DCM

The members of the Task Force have revised the DCM section after the analysis of the results of the Cardiomyopathy Trial (CAT).[5] This trial was designed to investigate whether ICDs would be effective in the prevention of all-cause death in patients with symptomatic DCM of recent onset (≤9 month), with severe impairment of left ventricular function (≤30%), but without documented symptomatic ventricular tachyarrhythmias. Sixty-five percent of patients were in NYHA class II and 35% in NYHA class III. The study was based on the assumption given in the literature that 1-year all-cause mortality would be 30%. It was estimated that enrollment of 1348 patients would be able to show a 1-year survival benefit of 6% for ICD with a power of 80% and a probability value of 0.05.

Table 2 Dilated cardiomyopathy

	Class I	Class IIa	Class IIb
Primary prevention	ACE-inhibitors Beta-blockers	Aldosterone receptor blockers	Amiodarone ICD
Secondary prevention	ICD ACE-inhibitors Beta-blockers	Aldosterone receptor blockers	Amiodarone

ACE—angiotensin converting enzyme; VTs—sustained ventricular tachycardia; VF—ventricular fibrillation; ICD—implantable cardioverter defibrillator; EF—ejection fraction

After inclusion of the first 100 of 1348 patients planned for inclusion, an interim analysis showed that all-cause mortality was 5.6%, which was much lower than the expected 30%; since the difference between the ICD and the control group was 2.6%, i.e. non-statistically significant, the trial was terminated earlier than planned.

CAT provides solid evidence that patients meeting the study entry criteria do not have a very poor short-term prognosis—this conclusion, however, should not be extended to DCM patients with different clinical characteristics. The findings of the study suggest that ICD is not indicated for primary prevention of sudden death in patients with DCM of recent onset, EF≤30% and no documented ventricular arrhythmias. Based on these data we now recommend the use of ICD in DCM no longer as a Class IIa but as a Class IIb indication with a level of evidence B (Table 2).

Conclusions

The 2002 Update of the guidelines for SCD prevention of the ESC has incorporated information derived from two clinical trials performed in patients with left ventricular dysfunction: MADIT II including patients with previous MI and EF≤30%, and CAT including patients with non-ischemic DCM and EF<30%. The results from the two studies are clearly divergent: while the presence of reduced EF in post-MI patients is sufficient to identify individuals at high risk of SCD and therefore supports the indication for an ICD, in patients with a similarly reduced EF of non-ischemic etiology (in the absence of documented arrhythmias), mortality is low and therefore no indication for an ICD is foreseen in this group of patients. The practical implication for clinicians is therefore the information that an ICD should be considered in post-MI patients with MADIT II clinical profile, while the results of MADIT II seem not applicable to patients with non-ischemic DCM. In the latter patients group the use of the ICD should be limited to patients with additional risk factors for SCD.

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