The implantable cardioverter defibrillator did not reduce mortality in ventricular arrhythmia

Connolly SJ, Gent M, Roberts RS, et al., for the CIDS Investigators. **Canadian Implantable Defibrillator Study (CIDS). A randomized trial of the implantable cardioverter defibrillator against amiodarone.** Circulation. 2000 Mar 21;101:1297-1302.

QUESTION

In patients surviving ventricular fibrillation or ventricular tachycardia (VT), is the implantable cardioverter defibrillator (ICD) better than amiodarone for prolonging survival?

DESIGN

Randomized (allocation concealed*), unblinded,* controlled trial with a mean follow-up of 3 years (Canadian Implantable Defibrillator Study [CIDS]).

SETTING

Centers in North America and Australia.

PATIENTS

659 patients (mean age 64 y, 85% men) who had documented ventricular fibrillation; out-of-hospital cardiac arrest requiring defibrillation or cardioversion; documented, sustained VT causing syncope; other documented, sustained VT (≥ 150 beats/min) causing presyncope or angina in patients with left ventricular ejection fraction ≤ 35%; or unmonitored syncope with subsequent documentation of either spontaneous VT ≥ 10 seconds or sustained (≥ 30 s) monomorphic VT induced by programmed ventricular stimulation. Exclusion criteria were recent acute myocardial infarction, electrolyte imbalance, contraindications to ICD or amiodarone, previous amiodarone therapy for ≥ 6 weeks, nonarrhythmic medical condition with poor prognosis, or long-QT syndrome. All patients were included in the analysis.

INTERVENTION

Patients were allocated to the ICD (n = 328) or to amiodarone, ≥ 1200 mg/d for ≥ 1 week in the hospital, ≥ 400 mg/d for ≥ 10 weeks, and ≥ 300 mg/d thereafter (n = 331).

MAIN OUTCOME MEASURES

Death from any cause. Secondary outcomes included death caused by arrhythmia.

MAIN RESULTS

Analysis was by intention to treat. Patients in the ICD group appeared to have a lower mortality rate relative to those in the amiodarone group, but the differences were not statistically significant (P = 0.14 for all-cause mortality; P = 0.09 for death from arrhythmia) (Table).

CONCLUSION

In patients with previous sustained ventricular arrhythmia, the implantable cardioverter defibrillator did not lead to fewer deaths than did amiodarone.

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*See Glossary.

Implantable cardioverter defibrillator (ICD) vs amiodarone for previous sustained ventricular arrhythmia†

Outcomes at mean 3 y	ICD	Amiodarone	Adjusted RRR (95% CI)	NNT (CI)
All-cause mortality	25%	30%	20% (–7.7 to 40)	Not significant
Death from arrhythmia	9.1%	13%	33% (–7.2 to 58)	Not significant

†Abbreviations defined in Glossary; RRR adjusted for left ventricular ejection fraction.

COMMENTARY

Two primary prevention trials (the Multicenter Automatic Defibrillator Implantation Trial [MADIT] [1] and the Multicenter Unsustained Tachycardia Trial [MUSTT] [2]) and 2 secondary prevention trials (Antiarrythmics versus Implantable Defibrillators [AVID] [3] and CIDS) have compared antiarrhythmic drugs with ICD therapy for treatment of potentially lethal ventricular arrhythmias. All 4 trials showed that ICDs are better for reducing cardiac and all-cause mortality.

In the CIDS trial, the relative risk reduction (RRR) in all-cause mortality for ICD was slightly short of statistical significance. However, most of this difference resulted from a reduction in deaths caused by arrhythmia, suggesting that ICD therapy has a higher efficacy. The AVID trial, which had a design similar to that of CIDS, was stopped early after showing a substantial relative reduction in all-cause mortality in the ICD group (39% at 1 y and 27% at 2 y). The 95% CIs in both studies are similar, which suggests that they represent a continuum, ranging from a modest to a marked advantage of ICD therapy over amiodarone to reduce cardiac mortality. A potential reason for the difference in the RRRs between AVID and CIDS may be found in the differential use of β-blocker therapy in the amiodarone group (16.8% in AVID and 23.7% in CIDS).

In a subsequent retrospective analysis of the CIDS data (4), all 659 patients in the study were stratified into 4 risk quartiles on the basis of reduced ejection fraction, advanced age, and New York Heart Association functional class. In highest-risk patients, ICD therapy led to an RRR of 50% for death when compared with amiodarone. No benefit from ICD therapy was seen in patients in the 3 lower-risk quartiles. Similar results were also reported for the AVID database, showing that the benefit of ICD implantation was more marked in the sickest patients with low ejection fraction and heart failure—despite the presence of concomitant nonarrhythmic mortality risks.

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