

An implantable cardioverter–defibrillator but not amiodarone reduced risk for death in congestive heart failure

Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med*. 2005;352:225-37.

Clinical impact ratings: GIM/FP/GP ★★★★★☆ Hospitalists ★★★★★☆ Cardiology ★★★★★☆

QUESTION

In patients with congestive heart failure (CHF), does amiodarone or an implantable cardioverter–defibrillator (ICD) reduce all-cause mortality more than placebo?

METHODS

Design: Randomized placebo-controlled trial (Sudden Cardiac Death in Heart Failure Trial [SCD-HeFT]).

Allocation: Concealed.*

Blinding: Blinded (clinicians and patients).*

Follow-up period: Median 46 months.

Setting: 145 centers in Canada and the United States.

Patients: 2521 patients who were ≥ 18 years of age (median age 60 y, 77% men) with New York Heart Association (NYHA) class II or III chronic, stable CHF from ischemic causes (left ventricular systolic dysfunction [LVSD] with marked coronary artery stenosis or documented myocardial infarction) or nonischemic causes (LVSD without marked stenosis); and an LV ejection fraction $< 35\%$.

Intervention: Amiodarone (loading dose of 800 mg daily for 1 wk, 400 mg daily for 3 wk, then a weight-dependent daily dose [200 to 400 mg]) ($n = 845$); a single-chamber ICD device programmed to shock-only mode (model 7223, Medtronic) with a detection rate of ≥ 187 beats/min for only rapid, sustained ventricular tachycardia or ventricular fibrillation ($n = 829$); or placebo ($n = 847$).

Outcomes: All-cause mortality and adverse effects.

Patient follow-up: 100% (intention-to-treat analysis).

MAIN RESULTS

70% of patients had NYHA class II CHF and 30% had class III CHF. 188 patients (11%) from the amiodarone and placebo groups crossed over to some form of ICD therapy. 259 patients in the ICD group (31%) received shocks from their device for any cause. Fewer patients who received ICD died from any cause than did those who received placebo (Table). Amiodarone and placebo groups did not differ for all-cause mortality (Table). Compared with placebo, amiodarone increased tremor ($P = 0.02$) and hypothyroidism ($P < 0.001$). In patients with NYHA class III CHF, ICD and placebo groups did not differ for mortality (hazard ratio [HR] 1.16, 97.5% CI 0.84 to 1.61); amiodarone increased mortality more than placebo (HR 1.44, CI 1.05 to 1.97). In

patients with NYHA class II CHF, amiodarone and placebo groups did not differ for mortality (HR 0.85, CI 0.65 to 1.11); ICD decreased mortality more than placebo (HR 0.54, CI 0.40 to 0.74).

CONCLUSIONS

In patients with congestive heart failure (CHF), a conservatively programmed, shock-only implantable cardioverter–defibrillator reduced all-cause mortality. Compared with placebo, ICD reduced mortality in New York Heart Association (NYHA) class II but not class III CHF. Amiodarone had no effect in NYHA class II CHF, and increased mortality in NYHA class III CHF.

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*See Glossary.

Amiodarone or a conservatively programmed, shock-only implantable cardioverter–defibrillator (ICD) vs placebo for congestive heart failure at median 46 months†

Outcome	Amiodarone	ICD	Placebo	RRR (95% CI)	NNT (CI)
All-cause mortality	9.5%	–	9.7%	1.6% (–16 to 17)	Not significant
	–	7.2%	9.7%	25% (10 to 38)	41 (25 to 108)

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

The SCD-HeFT trial provides evidence for prophylactic use of ICDs. The historical importance of SCD-HeFT and its effect on clinical practice must account for the trial's immediate influence on Medicare guidelines. SCD-HeFT reinforced earlier studies on the use of prophylactic ICDs in ischemic and nonischemic cardiomyopathy (1, 2). The inclusion and exclusion criteria of SCD-HeFT were rapidly incorporated into Medicare's reimbursement plan. According to the Centers for Medicare and Medicaid (CMS), these changes in ICD eligibility will increase the number of potential ICD patients by one third, to a total of 500 000 (3). CMS also mandated that the single-chamber, less-expensive ICD that was used in SCD-HeFT be used unless otherwise justified. Despite using single-chamber ICDs, the diagnosis-related group cost of U.S. \$25 000 to \$30 000 per ICD is still a concern.

SCD-HeFT also included an amiodarone arm, which showed no benefit in the primary prevention of sudden cardiac death (SCD). The large size of the SCD-HeFT trial clarifies questions asked by previous

smaller and sometimes conflicting studies of amiodarone for SCD prophylaxis. This lack of survival benefit will probably end almost a decade of research in SCD prevention with amiodarone. Although the SCD-HeFT trial provided many answers in SCD prevention, the methods used to identify patients with the highest risk are still primitive. Further trials will help determine whether the specific exclusions of SCD-HeFT have biological meaning and justification as implantation and reimbursement criteria.

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References

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