

# Amiodarone reduced arrhythmic death but not cardiac death in patients with MI and depressed left ventricular function

Julian DG, Camm AJ, Frangin G, et al., for the European Myocardial Infarct Amiodarone Trial Investigators. **Randomised trial of effect of amiodarone on mortality in patients with left-ventricular dysfunction after recent myocardial infarction: EMIAT.** *Lancet.* 1997 Mar 8; 349:667-74.

## Objective

To evaluate the effect of amiodarone on all-cause mortality, cardiac mortality, and arrhythmic death in survivors of a myocardial infarction (MI) with depressed left ventricular function.

## Design

Randomized, double-blind, placebo-controlled trial with a median 21-month follow-up.

## Setting

75 coronary care units in 15 European countries.

## Patients

1486 patients between 18 and 75 years of age (mean age 60 y, 84% men) who had had an MI and had a left ventricular ejection fraction (LVEF)  $\leq$  40%. Exclusion criteria were use of amiodarone in the previous 6 months, bradycardia, second- or third-degree atrioventricular block, sinus pauses

## Commentary (continued from page 142)

Although committees try to distinguish arrhythmic or sudden death from other types of cardiac death, assessments using these end points fail because sudden death and arrhythmic death overlap but are not identical. Some sudden deaths are caused by ventricular arrhythmia, but others are caused by re-infarction, pulmonary embolism, and bradycardia, for example (3). Inconsistency between committees in classifying deaths (4) also hampers systematic review. Therefore, the objective end point, total mortality, remains clinically the most useful.

The results of CAMIAT and EMIAT show that, unlike other antiarrhythmic drugs, amiodarone does not shorten life. Although these trials suggest that amiodarone decreases arrhythmic death, it failed to decrease total

> 2.5 seconds unless controlled by a pacemaker, hepatic disease, history of thyroid dysfunction, long QT syndrome, severe angina, or congestive heart failure refractory to conventional therapy, a need for antiarrhythmic therapy other than  $\beta$ -blockers or digoxin, need for cardiac surgery, contraindications to amiodarone, or childbearing potential. 2 patients were lost to follow-up.

## Intervention

743 patients were allocated to amiodarone, 800 mg/d for 14 days followed by 400 mg/d for 14 weeks and then 200 mg/d until the end of the study. 743 patients were allocated to placebo.

## Main outcome measures

All-cause mortality, cardiac mortality, and arrhythmic death.

## Main results

Analysis was by intention to treat. 205 patients died; 174 cardiac deaths occurred, of which 83 were arrhythmic. All-cause mortality ( $P = 0.96$ ) (Table) and cardiac mortality (85 vs 89) did not differ between the treatment groups. 33 patients in the amiodarone group had an arrhythmic death compared with 50 patients in the placebo group ( $P = 0.05$ ) (Table).

## Conclusion

Amiodarone reduced arrhythmic death but not all-cause mortality or cardiac mortality in survivors of a myocardial infarction with depressed left ventricular function.

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## Amiodarone vs placebo\*

Outcome at median 21 months	Amiodarone EER	Placebo CER	RRR (95% CI)	ARR  EER - CER  (CI)	RRI (CI)	ARI (CI)
Arrhythmic deaths	4.4%	6.7%	35% (0 to 58)	2.3% (0 to 4.7)	—	—
All-cause mortality	13.9%	13.7%	—	—	1.0% (-30.1 to 21.6)	0.2% (-3.7 to 3.4)

\*Abbreviations defined in Glossary; RRR, ARR, RRI, ARI, and CI calculated from data in article.

mortality in both trials. The clinical effectiveness of amiodarone in prolonging life after MI therefore remains unproved. To evaluate whether amiodarone decreases total mortality requires a larger, more costly trial, or in the interim, a meta-analysis of current trials. Physicians must also weigh the substantial adverse effects of amiodarone against any apparent benefit. The evidence does not justify the routine use of amiodarone in survivors of MI who have left ventricular dysfunction or asymptomatic ventricular arrhythmias.

On average, only half of the patients in these trials were receiving  $\beta$ -adrenergic blockers and ACE inhibitors, although these drugs are proven to increase survival (1). Instead of considering amiodarone to lower the risk for arrhythmic death, physicians should confi-

dently prescribe a  $\beta$ -adrenergic blocker or an ACE inhibitor to survivors of MI where appropriate.

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