ACP JOURNAL CLUB

THERAPEUTICS

Review: Implantable cardioverter defibrillators reduce all-cause mortality in nonischemic cardiomyopathy

QUESTION

In patients with nonischemic cardiomyopathy, is an implantable cardioverter defibrillator (ICD) more effective than medical therapy for preventing all-cause mortality?

METHODS

Data sources: MEDLINE (1966 to April 2004); EMBASE/Excerpta Medica (1991 to June 2004); the Cochrane Library and Central Register of Controlled Trials (current through the first quarter of 2004); bibliographies of relevant articles; and reviews, commentaries, and proceedings from national cardiology meetings (2003 to 2004).

Study selection and assessment: Randomized controlled trials (RCTs) that compared an ICD with medical therapy in patients resuscitated from cardiac arrest, documented or symptomatic sustained ventricular tachyarrhythmia, or depressed left ventricular function deemed to be at high risk for lethal cardiac arrhythmia. RCTs were also required to have recorded all-cause mortality, cardiac death, or arrhythmic mortality as the main outcome. All qualifying RCTs were assessed for adequate blinding of randomization, completeness of follow-up, and objectivity of the outcome assessment. **Outcome:** All-cause mortality.

MAIN RESULTS

ICD for primary prevention of cardiac arrhythmia: 5 RCTs (*n* = 3244) met the selection criteria. Meta-analysis (using a fixed-effects model) of the 5 RCTs (1854 patients with nonischemic cardiomyopathy) showed a greater reduction in mortality in the ICD group than in the medical-therapy group (relative risk reduction [RRR] 31%, 95% CI 13 to 45).

ICD for secondary prevention of cardiac arrhythmia (i.e., enrolled patients with previous resuscitated cardiac arrest or symptomatic ventricular tachycardia): 3 RCTs (*n* = 1963) met the selection criteria. Meta-analysis (using a fixed-effects model) of 2 RCTs (256 patients with nonischemic cardiomyopathy) showed that the groups did not differ for rates of all-cause mortality (RRR 31%, CI −24 to 61). Meta-analysis (using a fixed-effects model) of both the 5 primary and 2 secondary RCTs combined (2110 patients with nonischemic cardiomyopathy) showed a greater reduction in mortality in the ICD group than in the medical-therapy group (RRR 31%, CI 14 to 44). Use of a random-effects model or removing 1 RCT at a time did not have a substantial effect on the findings.

CONCLUSION

In patients with nonischemic cardiomyopathy, an implantable cardioverter defibrillator is more effective than medical therapy for reducing all-cause mortality.

For correspondence: Dr. A.S. Desai, Brigham and Women's Hospital, Boston, MA, USA. E-mail adesai@partners.org. ∎

COMMENTARY

Whereas coronary artery disease is common among patients who die suddenly, fatal arrhythmias cause a substantial portion of deaths in nonischemic heart failure (1). However, previous studies of ICDs have mainly focused on patients with ischemic heart failure. The meta-analysis by Desai and colleagues is timely because it examined whether an ICD reduces all-cause mortality in patients with nonischemic cardiomyopathy. Although it is preferable to make decisions using evidence from pivotal RCTs of the population in question, the use of a meta-analysis helps in situations exactly like this—a highly important observed risk and an intervention proven to be effective elsewhere yet less definitive in individual studies because of small subgroup sample sizes. By systematically aggregating the results of 7 RCTs, the authors showed a significant 31% survival benefit of ICDs over medical therapy.

In any meta-analysis, it is important to consider several limitations. First, a meta-analysis does not substitute for an RCT that is adequately powered to answer the question. However, until such trials are done, reviews like this one by Desai and colleagues assist in clinical decisions, especially when consistency across studies exists, as is the case here. Second, the results of a meta-analysis can be heavily influenced by 1 or a few studies. It is noteworthy that the results of Desai and colleagues remained consistent after excluding individual RCTs or when studies were analyzed in 2 subgroups (primary vs secondary prevention). A third limitation is publication bias, which is less likely in this case because ICDs are too expensive for such trials to go unnoticed, even without a publication record. Finally, the authors did not have access to patient-level data. However, only RCTs were included, which presupposes that potential confounders were evenly distributed between the ICD and medical-therapy groups.

Despite the potential limitations, Desai and colleagues have made an important contribution to the growing body of evidence suggesting that ICD use is beneficial in both ischemic and nonischemic cardiomyopathy. However, with only 2110 patients studied, several questions remain unanswered on ICD use in nonischemic cardiomyopathies, especially the costs involved. Whereas infarct scar seems to be important for sudden death in ischemic cardiomyopathies, the exact mechanism is less clearly understood in nonischemic cardiomyopathies. Thus, future work should focus on how sudden death occurs in nonischemic cardiomyopathies and the development of diagnostic tests to guide clinicians in identifying patients with the highest risk for an arrhythmic death who would derive maximum benefit from an ICD.

Adrian F. Hernandez, MD
Duke University Clinical Research Institute
Durham, North Carolina, USA

Reference
1. **Josephson M, Wellens HJ.** Implantable defibrillators and sudden cardiac death. Circulation. 2004;109:2685-91.