Prevalence and Clinical Course of Patients in Spain With Acute Myocardial Infarction and Severely Depressed Ejection Fraction Who Meet the Criteria for Automatic Defibrillator Implantation

Julio Martí Almor, Marta Delclós Baulies, Joaquim Delclós Urgell, Josep Comín Colet, Mercè Cladellas Capdevila, and Jordi Bruguera Cortada

Unidad de Arritmias, Servicio de Cardiología, Hospital del Mar, Barcelona, Spain.

The Multicenter Automatic Defibrillator Implantation Trial (MADIT)-II has broadened the indications for cardioverter defibrillator implantation. We present a retrospective study designed to estimate the number of patients in Spain eligible for an implantable defibrillator according to the MADIT-II criteria. From January 1999 to October 2002, 758 consecutive patients were admitted to our center with the diagnosis of acute myocardial infarction. Sixty-seven had a left ventricular ejection fraction ≤30% (mean, 23[5]) and were not eligible for revascularization. Excluding patients older than 80 years and patients with marked co-morbidity, 47 patients met the MADIT-II criteria for an implantable defibrillator. After a mean follow-up of 18 months, there were 20 deaths, 6 of which were considered sudden. In conclusion, application of the MADIT-II criteria for defibrillator implantation may benefit 6% of the patients with myocardial infarction in Spain. This proportion translates as 4110 defibrillator implantations.

Key words: *Sudden death. Implantable defibrillator. Infarction.*

Full English text available at: www.revespcardiol.org

Prevalencia y evolución en España de los pacientes con infarto agudo de miocardio y fracción de eyección severamente deprimida,con criterios de implantación de desfibrilador automático

El Multicenter Automatic Defibrillator Implantation Trial (MADIT) II amplía las indicaciones de los desfibriladores automáticos implantables. Presentamos un estudio retrospectivo que tiene como objetivo conocer el número de pacientes con criterios MADIT-II en nuestro entorno. Entre enero de 1999 y octubre de 2002, 758 pacientes fueron ingresados en nuestro servicio por un infarto agudo de miocardio. En 67 pacientes, la fracción de eyección fue ≤ 30% y no eran revascularizables. La fracción de eyección media de este grupo fue del 23 ± 5%. Si excluimos a los pacientes de más de 80 años y a los que presentaban una marcada morbilidad asociada, 47 pacientes hubieran cumplido los criterios MADIT-II (6%). En un seguimiento medio de 18 meses hubo 20 muertes, 6 de ellas de forma súbita. Si extrapolamos estos datos a nuestro país, el número anual de implantes se incrementaría hasta unos 4.110.

Palabras clave: *Muerte súbita. Desfibrilador implantable. Infarto.*

INTRODUCTION

Indications for implantable cardioverter defibrillator (ICD) implantation are well established in the 1998 guidelines of the American College of Cardiology/American Heart Association (AHA/ACC) and NASPE[1] and barely differ from the Spanish Society of Cardiology 1999 guidelines.[2] The AHA/ACC guidelines have been updated[3] to reflect data from the March 2002 Multicenter Automatic Defibrillator Implantation Trial (MADIT) II report,[4] and other trials. The MADIT-II study of primary prevention of sudden death applied only 2 criteria in patient enrolment: presence of ischemic heart disease and severe left ventricular dysfunction with ejection fraction (EF) ≤30%. This indication was included in the revised AHA/ACC guidelines as sufficient scientific evidence of level 2A.[3] The MADIT-II authors estimate that 10%

Correspondence: Dr. J. Martí Almor.
Servicio de Cardiología. Hospital del Mar.
Pg. Marítim, 25-29. 08003 Barcelona. España.
E-mail: jmarti@imas.imim.es

Received August, 20 2003.
Accepted for publication March, 3 2004.

ABBREVIATIONS

ICD: implantable cardioverter defibrillator.
EF: ejection fraction.
MI: myocardial infarction.
MADIT: multicenter automatic defibrillator implantation trial.
SD: standard deviation.
95% CI: 95% confidence interval.

of patients with ischemic heart disease in the United States probably meet ICD implantation criteria. In Spain, the number of patients who might benefit from this indication is unknown and may well differ as a factor of our national context.

The objective of this study was to determine the proportion of patients with myocardial infarction (MI) who present MADIT-II criteria and their evolution.

PATIENTS AND METHODS

This is a retrospective, observational, cohort study. From January 1999 thru October 2002, we enrolled 758 consecutive patients admitted to our cardiology service in Barcelona, Spain, and diagnosed with MI on the basis of clinical criteria, ECG and enzyme levels (creatine kinase [CK] and creatine kinase MB fraction [CK-MB]). Of these, 67 patients (8.8%) were ineligible for surgical or percutaneous revascularization and had EF≤30%. Ejection fraction was determined by echocardiogram or radioactive isotope or contrast ventriculography during coronary angiography carried out >2 months after MI to avoid myocardial stunning.

Most patients attended follow-up clinics at our center every 5-7 months. Only 14 patients did not attend and follow-up telephone calls were made to individual patients or the families of patients who had died.

Statistical Analysis

Continuous variables are expressed as mean and standard deviation (SD) and categorical variables as percentage. Confidence intervals (CI) are calculated using the exact method according to the binomial law.

RESULTS

Mean age of the 67 patients with MI and EF≤30% was 67±24 years, 50 (75%) were men, 43 (64%) had previous MI, 27 (40%) had MI with ST-segment elevation, and 61 (91%) had disease in 3 vessels. Fifteen patients (22%) with EF>30% had undergone revascularization following MI (9 percutaneous and 6 surgical procedures).

At discharge, patients were prescribed aspirin (98%), beta-blockers (72%), ACE inhibitors or angiotensin II receptor antagonists (65%), amiodarone (16%) in connection with paroxysmal atrial fibrillation, and diuretics (27%) of which 60% had spironolactone. Mean functional class at discharge was 2.5±0.8. Mean EF was 23±5% (range, 12%-30%). Nine patients underwent Holter monitoring for the prevention of sudden death but none presented nonsustained ventricular tachycardia and electrophysiological studies to discount their meeting MADIT[5] criteria were not performed. The ECG studies of the 67 patients showed a mean QRS complex width of 124±27 ms.

After 18±7 months mean follow-up, 2 patients had undergone ICD implantation as secondary prevention on classical indications: 1 showed intolerance of sustained monomorphic ventricular tachycardia and another suffered heart failure on recovery from ventricular fibrillation with neurological after-effects. Among the remaining 65 patients, ICD implantation was not considered in 19 patients: 14 were >80 years old and 5 had concomitant diseases with a life expectancy <1 year. Only 1 patient was lost during follow-up. Consequently, 47 patients (70%) met MADIT-II criteria for ICD implantation, which is 6% of patients with MI admitted to our center.

Total mortality among these 47 patients was 42% (20 patients). However, 2 patients required ICD implantation during follow-up and should be included in the sudden death group. Thus, the distribution of patient deaths would be 8 (6+2) due to sudden death, 10 due to reinfarction or progression of heart failure, and 3 due to noncardiac diseases (2 neoplasias and 1 intestinal ischemia); 1 death was due to unknown cause. Mean time from diagnosis of infarction to death was 8±3 months for sudden death and 12±6 months for death due to all other causes.

Only one of the 6 sudden death events was witnessed as this patient died in the street. Ventricular fibrillation was recorded with recovery and irreversible neurological damage. The other 5 patients died at home at night and autopsy study results are not available. Consequently, other causes of death (e.g. reinfarction, stroke or pulmonary thromboembolism) cannot be ruled out. Among these 47 patients, ICD implantation might have avoided between 3 and 8 sudden death events, a reduction in risk of death of between 6.4% (95% CI, 1.3-17.5), and 17% (95% CI, 7.6-30.8).

DISCUSSION

The results of this retrospective cohort study suggest some 6% of patients diagnosed with MI on admission to hospital might benefit from ICD implan-

tation according to MADIT-II criteria. Characteristics of our patients are very similar to MADIT-II patients in terms of age, EF, QRS interval width and medical treatment followed. However, there are relative differences in the percentage of patients revascularized and in the cutoff point for age (we excluded patients >80 years from ICD implantation for primary prevention). Including these patients may be feasible in the United States but it is difficult to justify within the Spanish public health system. If we discount patients >80 years (n=14), only 2 of whom underwent percutaneous revascularization, 13 (28%) of the remaining 47 patients underwent post-infarction revascularization and none of them required primary angioplasty. A strategy of primary angioplasty would probably have reduced the number of patients with EF≤30% to just 2 (9%) as reported by González Carrillo et al.[6]

The implantation of ICDs in the 47 eligible patients could have avoided up to 8 sudden death events, assuming that these were arrhythmic events, which has only been confirmed in 3 patients. Nevertheless, our results indicate that although ICD implantation as primary prevention of sudden death in this population might have reduced arrhythmic death, the strategy would raise costs as patients receiving an ICD would die of causes the ICD cannot prevent (in our case, 14 of 20 deaths).

If we extrapolate our data to Spain as a whole, where the number of infarctions in 2002 was 68 500,[7] some 4110 patients (6%) might benefit from ICD implantation. This would be a significant increase on the current number of defibrillator implants if we add together those used in primary and secondary prevention, although up-to-date data on the number of implants have not been published. Spain's National Registry of Defibrillators for 1996[8] records some 332 implants per year. However, results of important studies such as the Antiarrhythmic Versus Implantable Defibrillators (AVID) trials,[9] the Canadian Implantable Defibrillator Study (CIDS),[10] the Multicenter Unsustained Tachycardia Trial (MUSTT),[11] or MADIT itself,[5] cannot have influenced the growth in indications occurring from 1996 to the time of writing. In 1996, 9 ICD implantations were performed per million inhabitants per year, a figure comparable to that of countries such as the United Kingdom,[7,12] where the number of ICD implants has increased to 41 per million inhabitants per year in 2001.[14] Although we know geographic differences occur in ICD implantation in Europe,[13] if we apply UK growth to Spain, we can predict an annual rate figure of 1600 ICD implantations per year.

Unpublished data obtained from industrial sources indicate that 1477 ICDs were implanted in Spain in 2002, which is not so very far from this projection.

Growth from 1477 to 4110 ICD implantations per year would mean a notable increase in public health costs. However, the 31% reduction in mortality that applying MADIT-II criteria would bring about, together with a consequent reduction in ICD costs, would help to spread the benefits of this study.

To summarize, 6% of patients admitted with MI could benefit from ICD implantation on MADIT-II criteria. This could produce a considerable reduction in mortality at 18 months.

Limitations of the Study

In addition to the limitation inherent in any retrospective study, we must assert that a population of post-infarction patients with 45%-58% revascularizations and an age limit such as that included in MADIT-II is not the same as a population with 28% revascularizations, from which patients >80 years have been excluded. Consequently, the results of this study should be read with caution. We need to perform a nationwide, prospective study to determine the prevalence of MADIT-II patients with greater precision.

ACKNOWLEDGEMENTS

The authors wish to thank Dr Jaume Marrugat for his comments on an early draft of the manuscript.

REFERENCES

1. ACC/AHA guidelines for implantation of cardiac pacemakers and antiarrhythmia devices: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on pacemaker implantation). J Am Coll Cardiol 1998;3:1175-209.
2. Pérez-Villacastín J, Carmona Salinas JR, Hernández Madrid A, Marín Huerta E, Merino Llorens JL, Ormaetxe Merodio J, et al. Guías de práctica clínica de la Sociedad Española de Cardiología sobre el desfibrilador automático implantable. Rev Esp Cardiol 1999;52:1083-104.
3. Gregoratos G, Abrams J, Epstein AE, Freedman RA, Hayes DL, Hlatky MA, et al. ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices. Circulation 2002;106:2145-61.
4. Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannon DS, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med 2002;346:877-83.
5. Moss AJ, Hall J, Cannon DS, Daubert JP, Higgins SL, Klein H, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. N Engl J Med 1996;335:1933-40.
6. Gonzalez Carrillo J, García Alberola A, Saura Espín D, Carrillo Sáez P, López Palop R, Sánchez Muñoz JJ, et al. Impacto de la angioplastia primaria en la indicación de desfibrilador implantable en pacientes con infarto de miocardio. Rev Esp Cardiol 2003; 56:1182-6.
7. Marrugat J, Elosua R, Martí H. Epidemiología de la cardiopatía isquémica en España: estimación del número de casos y de las

tendencias entre 1997 y 2005. Rev Esp Cardiol 2002;55:337-46.
8. Madrid AH, Cinca J, Moro C. Registro nacional de desfibriladores automáticos implantables en 1996. Rev Esp Cardiol 1998; 51:349-55.
9. The Antiarrhythmics versus implantable defibrillators (AVID) investigators. A comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from near fatal ventricular arrhythmias. N Engl J Med 1997;337: 1576-83.
10. Roy D, Talajic M, Tang A, Dubuc M, Gardner M, Thibault B, et al. Mode of death in the Canadian Implantable Defibrillator Study (CIDS). Circulation 1998;17(Suppl):2606.
11. Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G. A randomized study of the prevention of sudden cardiac death in patients with coronary artery disease. N Engl J Med 1999;341:1882-90.
12. Ector H, Rickards AF, Kappenberger L, Linde C, Vardas P, Oto A, et al. The world survey of cardiac pacing and implantable cardioverter defibrillators: calendar year 1997-Europe. PACE 2001; 24:863-8.
13. Ovsyshcher E, Furman S. Determinants of geographic variations in pacemakers and implantable cardioverter defibrillators implantation rates. PACE 2003;26:474-8.
14. Plummer CJ, Irving RH, McComb JM. Implications of national guidance for implantable cardioverter defibrillation implantation in the United Kingdom. PACE 2003;26:479-82.