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Brief report

Defibrillator Implantation for the Primary Prevention of Sudden Death in Patients Awaiting Cardiac Transplantation: One Center's Experience

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ABSTRACT

Patients who are on a waiting list for cardiac transplantation often have a clinical profile that satisfies current recommendations for the implantation of an implantable cardioverter defibrillator (ICD) for the primary prevention of sudden death. The prospect that transplantation may take place within the short-to-medium term puts the effectiveness of this therapy in doubt. We investigated the incidence of therapy delivered by ICDs implanted for primary prevention in patients awaiting cardiac transplantation. Recent changes in the incidence of sudden death at our center were also investigated. Data on 308 patients listed for heart transplantation between 1998 and 2008 were reviewed. An ICD was indicated for primary prevention at initial evaluation in 17 patients. Of these, 53% received appropriate ICD therapy while carrying an ICD for a mean period of 7.8 ± 4.8 months. Only one patient received inappropriate therapy and none had any complications associated with device use. The frequency of sudden death has decreased over the course of recent years.

Implante de desfibrilador como prevención primaria de muerte súbita en pacientes en lista de espera de trasplante cardiaco: experiencia de un centro

Palabras clave:
Trasplante
Muerte súbita
Desfibrilador
Desfibrilador automático implantable
Prevención primaria

RESUMEN

Los pacientes incluidos en lista de espera de trasplante cardiaco frecuentemente presentan un perfil acorde con las recomendaciones actuales en cuanto al implante de desfibrilador automático implantable (DAI) como prevención primaria de muerte súbita. El eventual trasplante a corto-medio plazo hace dudar de la efectividad de dicha terapia. Analizamos la incidencia de terapias administradas por el desfibrilador implantado como prevención primaria en pacientes en lista, así como la evolución histórica en la frecuencia de muerte súbita en nuestro centro.

Se revisó a los 308 pacientes incluidos en lista desde 1998 hasta 2008. En 17 pacientes se indicó DAI como prevención primaria al momento de la inclusión. El 53% de éstos recibió terapias adecuadas, habiendo portado el dispositivo una media de 7,8 ± 4,8 meses. Sólo 1 paciente presentó terapias inadecuadas y ninguno sufrió complicaciones asociadas al dispositivo. La frecuencia de muerte súbita se ha reducido a lo largo de los últimos años.

INTRODUCTION

Patients included on the waiting list for heart transplantation often have a clinical profile which meets clinical guidelines recommending the use of an implantable cardioverter defibrillator (ICD) for primary prevention of sudden death (SD).[1] There is some debate as to whether results from large prospective studies (MADIT II,[2] SCD-HeFT[3]) that evaluated primary prevention of SD with ICD apply to these patients. Studies have shown that 19%–26% of patients on the waiting list would be candidates for ICD implantation according to the MADIT II study criteria, with that proportion rising to 58% using the SCD-HeFT criteria.[4,5] For years, ICDs have been implanted for primary prevention in patients on the transplantation waiting list, under the assumption that levels of efficacy and safety would be similar to those observed in the general population of patients with an indication for the device. However, the possibility of transplantation within the short-to-medium term may lead to doubts about the usefulness of the treatment, given that it is only used for a short time. The aim of this paper was to review the effectiveness and safety of ICD for primary prevention of SD in patients on the waiting list for elective heart transplantation. The incidence of appropriate and inappropriate therapies administered by the device was analyzed, together with concomitant complications from implantation until transplantation, exclusion from the waiting list, or the patient's death. In addition, we reviewed the historical development of ICD implantation and the incidence of SD in our center.

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METHODS

We retrospectively reviewed the records of 308 patients included on the waiting list for elective cardiac transplantation at our center from 1998, the year in which clinical guidelines contemplating the primary prevention of SD first appeared,[6] until January 2008. Until 2002, implants were considered as primary prevention when non-sustained ventricular tachycardia was shown by Holter studies to be present in patients with ischemic cardiomyopathy and left ventricular dysfunction or syncope, without a record of tachyarrhythmias. After 2002, ICD implantation also was treated as primary prevention in patients with an etiology of ischemic cardiomyopathy with severe ventricular dysfunction. In the last two years of the study period, patients with an indication for implantation based on cardiomyopathy of any etiology with severe systolic dysfunction and functional class III–IV were also included. ICDs were considered implanted at the time of waiting list inclusion if they were implanted between 6 months before and 3 months after the effective date of inclusion on the waiting list.

In the review of device use, appropriate therapy was defined as antitachycardia or defibrillation treatment administered for ventricular tachyarrhythmia which had not terminated spontaneously before the device administered the therapy. Appropriate treatment was identified from episode electrograms analyzed by expert staff. Inappropriate treatment was defined as antitachycardia or defibrillation therapy administered because of a supraventricular tachycardia or artifact. These were also identified by a review of stored electrograms. Complications potentially deriving from device implantation or during follow-up were also recorded.

RESULTS

The evolution of the 308 patients was as follows: 257 (83.4%) received transplants, 28 (9%) were excluded from the waiting list, 14 (4.5%) died while on the list (8 due to SD), and 9 were still on the list at the end of the follow-up period. Due to the expansion of the indications for ICD implantation included in international guidelines published in 2002,[7] the data were broken down into 2 periods: 1998–2002 and 2003–2008 (Table 1). The evolution of the 17 patients identified as ICD wearers, in which implantation was indicated for primary prevention at the time of inclusion on the waiting list, was as follows: 13 were transplanted, 2 were excluded because of improvement, and 2 were still on the list at the end of the follow-up. None of these patients died during follow-up. Table 2 shows the clinical characteristics and main prognostic variables of these 17 patients. All were in functional class III–IV at the time of evaluation for inclusion on the waiting list. The average time on the waiting list was 5.6 ± 4.5 months in this patient group. Mean time with the ICD was 7.8 ± 4.8 months.

Of these 17 patients, 9 (53%) received appropriate therapy administered by the ICD while they were wearing the device. When analyzed by time period, incidence of appropriate therapy was found to be 66% (2 patients) for the 1998–2002 period, compared to 50% (7 patients) in the 2003–2008 period. Only 1 patient received inappropriate therapy, in the context of atrial fibrillation with rapid ventricular response. No patients had complications associated with device implantation or during follow-up.

Table 1
Patients Included on the List During 1998–2008, Broken Down Into Two Periods

	Included on the list	Total ICD carriers	ICD for primary prevention	Sudden death
1998–2002	193	14 (7.3%)	3 (1.5%)	7 (3.6%)
2003–2008	115	43 (37.4%)	14[a] (12.2%)	1 (0.9%)
Total	308	57 (18.5%)	17 (5.5%)	8 (2.5%)

ICD, implantable cardioverter defibrillator.
[a] 3 patients with ICD-resynchronizer device.

Table 2
Patients' Clinical, Echocardiographic, and Hemodynamic Characteristics[a]

Age (years)	49 ± 12
Sex	Male 94% Female 6%
Etiology	Idiopathic 53% Ischemic 35% Valvular 6% Toxic 6%
LVEF (%)	20 ± 6
Right ventricular dysfunction	70%
Diastolic index (mm/m^2)	39 ± 7.3
Oxygen consumption (ml/kg/min)	14.9 ± 3
Mean pulmonary arterial pressure (mmHg)	32 ± 12
Cardiac index (l/min/m^2)	1.9 ± 0.4
Kidney failure[b]	0%
Elevated bilirrubin[c]	47%
Diabetes mellitus	17%
Hypertension	6%
Amiodarone	18%

LVEF, left ventricular ejection fraction.
[a] Values are mean ± standard deviation unless otherwise indicated.
[b] Creatinine > 1.5 mg/dL.
[c] Bilirrubin > 1 mg/dL.

DISCUSSION

The results of this study showed that the incidence of appropriate treatment when implanted ICDs were used as primary prevention in patients enrolled on the waiting list for heart transplantation was high, despite the short time wearing the device. On the other hand, the incidence of inappropriate treatment was low and the lack of complications indicated low risk to the patient. Information on the use of ICDs in patients on waiting lists for heart transplantation is limited to a few series, all of which were retrospective and included only a small number of patients. Selection criteria were not homogeneous, with indications for primary and secondary prevention intermixed. Sandner et al.[8] recruited 102 patients wearing an ICD while on a waiting list. Most of the devices had been implanted prior to assessment for inclusion on the waiting list and the indication was for secondary prevention. The rate of appropriate therapy was very high (66%), with a significant reduction in mortality (13% vs. 25%) compared to the control group (other patients on the waiting list, but without a defibrillator). Another study[9] showed similar results in terms of secondary prevention.

The use of ICD for primary prevention was reflected in a series of patients implanted with the device during evaluation for transplant.[10] The authors suggested that, in 19 of the 35 patients studied, the defibrillator had an off-label indication, (no evidence of syncope, tachyarrhythmia, and non-sustained ventricular tachycardia) which could be evidence of its use as primary prevention The incidence of therapy was 31%. Unlike the series reported in the present paper, recent indications based only on low left ventricle ejection fraction and advanced functional class were not collected. This is important given that, based on these criteria, defibrillator implantation would be indicated in a large number of

patients on the heart transplant waiting list. The efficiency of such a measure might be undermined by the limited time that the patient wears the device. Despite this, there is a high incidence of appropriate defibrillator treatment: the implantation of ICD as a "bridge to transplant" has been shown to be a very attractive means of reducing expected mortality (8% in Spain[11]). Among other advances in the treatment of such patients, the use of defibrillators probably helped reduce the incidence of SD in our series.

It is not possible to determine from the available data whether the arrhythmias treated by the device would have been fatal or not. However, given the high rate of deaths from SD (estimated at 25%–40%[12,13]) among patients on the heart transplant waiting list, it is conceivable that a not insignificant percentage of the episodes would have involved fatal arrhythmias without use of ICDs. Other limitations of our study include the small sample size and the fact that it was performed in only one center.

CONFLICTS OF INTEREST

None declared.

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