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Introduction and objectives. The purpose of this report is to present the results obtained with heart transplantation in Spain from the first use of this therapeutic modality in May 1984.

Methods. A descriptive analysis of all heart transplantations performed up to December 31, 2009 is presented.

Results. In total, 6048 transplants were carried out. The typical clinical profile of a Spanish heart transplant patient in 2009 was that of a 53-year-old male who had been diagnosed with nonrevascularizable ischemic heart disease and who had severely impaired ventricular function and a poor functional status. The implanted heart typically came from a donor who had died from a brain hemorrhage (mean age 37 years) and the average time on the waiting list was 106 days. Mean survival time has increased progressively over the years. Whereas for the whole time series, the probability of survival at 1, 5, 10 and 15 years was 78%, 67%, 53% and 40%, respectively, for the past 5 years, the probability of survival at 1 and 5 years was 85% and 73%, respectively. The most frequent cause of death was acute graft failure (17%), followed by infection (16%), the combination of graft vascular disease and sudden death (14%), tumor (12%) and acute rejection (8%).

Conclusions. The survival rates obtained in Spain with heart transplantation, especially in recent years, make the procedure the treatment of choice for patients who have irreversible heart failure and a poor functional status and for whom there are few other established medical or surgical options.

Key words: Heart transplantation. Registry. Survival.

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INTRODUCTION

This article is the customary annual update analysis describing results of heart transplantation (HT) activity conducted in Spain between the first such procedure, performed in May 1984, and December 31, 2009.1,2

This Registry includes data on all HTs performed by teams at all centers in Spain (Annex 1). It is, therefore, an accurate account of the status of heart transplantation in the country. The report’s reliability is founded on the nationwide use of a single database constructed on mutually agreed principles, which standardizes variables and the possible responses.

METHODS

Patients and Centers

Nineteen HT centers (Table 1) have supplied the Registry with data, although only 18 are currently active.

In the 25 years that HT procedures have been performed in Spain, the total number of operations has reached 6048. Figure 1 presents the distribution of the number of HTs per year. Of these, 94% were isolated orthotopic transplants. Table 2 shows the distribution of transplants by procedure type.

Design

The database includes 175 clinical variables with data on recipients, donors, surgery, immunosuppression and follow-up. Each year, the centers send data to the Registry Director, who organizes the statistical methodology with the company contracted to perform the analysis. The Director is also responsible for organizing the audit of centers to verify data which is conducted by an independent external company that randomizes the centers and HTs, extracts a representative sample, and confirms the reliability of the data submitted.

In 2008, the Registry was presented to, and received the approval of, the Committee for Biomedical Research Ethics of the Hospital Universitario La Fe, Valencia. We are in the process of submitting the Registry to the Spanish Ministry of Health and Consumer Affairs to guarantee fulfillment of Spanish Data Protection Law 15/1999.

Statistical Analysis

Variables are presented as mean (SD). Data on survival are analyzed in Kaplan-Meier curves and compared using the log-rank test. A $P$ value of <.05 was considered significant.
RESULTS
Heart Transplant Recipient Profile

In Spain, the profile of the average HT recipient is that of a 53-year-old man diagnosed with ischemic heart disease or idiopathic dilated cardiomyopathy and with blood group A or O. Table 3 shows the clinical profile of isolated HT recipients by age-group; retransplantation recipients appear in a separate column.

Waiting List Mortality and Days to Transplant

In 2009, waiting list mortality was 7%. The percentage of patients excluded from transplantation after inclusion on the waiting list was 16%. Figure 2 shows the annual percentage of waiting list patients who received an HT, were removed from the list without receiving one, or died before receiving one. Mean waiting list time for recipients prior to undergoing HT in 2009 was 106 days. Figure 3 shows how this has evolved over the last 18 years.

Cause of Death and Mean Donor Age

Most HT donors die of cerebral hemorrhage. Mean donor age in 2009 was 37 years (Figures 4 and 5).

Urgent Transplantation

The rate of indication for urgent transplantation in 2009 was 38%. Figure 6 shows the evolution of indication for urgent HT over the years.
2005, it was 10% and since then it has increased by a mean 7%.

When survival rate data for 2009 were added to those of previous years, we obtained 88% 1-month actuarial survival and 1-, 5-, 10-, and 15-year rates of 78%, 67%, 54% and 41%, respectively (Figure 11). Survival by periods showed better results in the latter stages with survival rates at 1 and 5 years of 85% and 73%, respectively (Figure 12).

Survival curves differed according to the etiology indicating HT (Figure 13). Degree of urgency influenced probability of survival (Figure 14).

**Causes of Death**

The most frequent cause of death was early graft failure (17%), followed by infection (16%), combined graft vascular disease and sudden death (14%), tumors (12%) and acute rejection (8%) (Figure 15). When causes of death are distributed by periods, differences can be seen at ≤30 days (acute graft
failures), 1-12 months (infection), and >1 year (tumors, the combination of sudden death with chronic rejection and infection). Figure 16 shows the distribution of causes of death by periods.

**DISCUSSION**

With 25 years’ experience of HT in Spain, and over 6000 transplants performed, we would say that this
An important advantage of the Spanish Heart Transplantation Registry is that it is compiled from a standardized database to which all Spanish Transplant Teams submit data. They update annually and send figures to the Registry Director for collation and submission to an independent statistics consultancy for analysis. We believe procedure can be offered to the population at large in the certainty that levels of knowledge, control, and survival are similar to or better than those of other countries in western Europe and around the world. Analysis of the Registry of the International Society for Heart and Lung Transplantation annual report demonstrates this clearly.\textsuperscript{21-24}
The fact that, in Spain, centers are authorized to conduct HTs without adequate needs analysis is of great concern to the Transplant Teams because as the number of optimal donors has shown a clear downward trend, the HT/center ratio is falling, too. The fact that fewer HT procedures are being performed leads to under use of resources in hospitals equipped to conduct a great number of transplants, and to a longer learning process needed to achieve adequate results. The only tangible benefit for patients is the convenience of being able to undergo transplantation without having to travel far from home.

In 2009, the number of HTs performed declined (274 in 2009 vs 292 in 2008). This is not particularly worrying as it fits the pattern of recent years. What is of greater concern is the progressive fall in the number of HTs performed over the years.

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Again because they die after being removed from the list. According to Spain’s national transplant organization, these accounted for some 8% of deaths in 2009. Consequently, in 2009 mortality among patients with advanced heart failure and waiting for a heart was 15%.

The clinical profile of patients has not changed in recent years. We analyzed HT recipients in 3 groups (pediatric, adult and retransplantation) as each of these is indicated for transplant for very different clinical causes: pediatric patients are operated...
for congenital heart disease or idiopathic dilated cardiomyopathy; they have higher pulmonary resistances and present no cardiovascular risk factors. In contrast, patients undergoing retransplantation are usually indicated for graft vascular disease; they present greater organ deterioration and more risk factors. This may be a more accurate explanation for the bad prognosis of these patients than the fact that they undergo a second transplant.

Urgent HT is somewhat controversial, as these operations have specific characteristics (recipients in worse clinical condition, less-than-ideal donors, longer periods of ischemia) that entail a worse prognosis than programmed transplants. In 2009, the percentage of urgent HTs rose by 6% (38% in 2009 vs 32% in 2008). The percentage of patients undergoing urgent HT varies from one geographical area to another and alters substantially from one year to the next. Why indication for urgent HT fluctuates like this is unclear and differences in geographical distribution are also difficult to explain, although low donor numbers and improved care of critical patients (ventricular assist device implants) increase opportunities for urgent HT. Indication for

![Figure 13. Survival curves according to etiology indicating transplantation.](image1)

![Figure 14. Survival curves by degree of urgency.](image2)

In the last 5 years, approximately half the urgent HT recipients had previously had some sort of ventricular assist implant. These devices are crucial to the care and stabilization of patients with acute heart failure prior to transplantation, so it is advisable that Transplant Teams should have access to them for more critical patients.

Induction immunosuppression is used in most HT procedures. Since transplantation was first performed, the most frequent treatment has been with OKT3 antilymphocyte antibodies (35% of the entire series) although currently interleukin 2 antagonists are more common (85% of HTs performed in the last 5 years). The most frequently used maintenance immunosuppression treatment is known as the triple combination: cyclosporine versus tacrolimus, azathioprine versus mycophenolate mofetil, and steroids. However, depending on patient clinical course, the introduction of other immunosuppressors has been questioned, given that it offers clearly poorer results. However, the Transplant Teams consider that this option should continue to exist although in a controlled form. To ensure optimal chances of survival for critical patients undergoing transplantation we should bear in mind, as European guidelines on heart failure recommend, that it is better to stabilize heart failure than indicate for urgent HT, and that transplantation should not be considered a treatment for unstable acute heart failure among other things, because of the time taken in locating a donor even in cases as urgent as these.

At HT, the percentage of patients with some type of ventricular assist implant has gradually increased, especially in the last 5 years. The intraaortic counterpulsation balloon is the most frequently used device. The use of extracorporeal membrane oxygenation and pulsatile devices has increased substantially, too. In the last 5 years, approximately half the urgent HT recipients had previously had some sort of ventricular assist implant. These devices are crucial to the care and stabilization of patients with acute heart failure prior to transplantation, so it is advisable that Transplant Teams should have access to them for more critical patients.

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CONCLUSIONS

In general, early and late survival rate figures are similar to those published in international registry reports and have improved year by year, especially in the last 5 years.

We should continue to try to reduce the high incidence of early graft failure, as this would have a particularly good effect on the probability of immediate post-operative and overall survival.

Given that infection is a greater cause of morbidity and mortality than rejection, we should pay it more attention and situate it among the principle objectives of general studies and clinical drug trials.

REFERENCES


ANNEXE 1 Spanish Heart Transplantation Teams Contributing to the Spanish Heart Transplantation Registry 1984-2009

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