This paper describes the general situation regarding heart transplantation in Spain and the results obtained using the technique, incorporating data for the year 2004. In 2004, 294 heart transplants were carried out, which brings the total number of procedures performed since 1984 to 4680. Clinically, the typical heart transplant recipient in Spain is male, aged around 50 years, has blood group A, has non-revascularizable coronary artery disease, and is in NYHA functional class IV/IV. The percentage of emergency heart transplantations was 35%, which is higher than in the previous year (29%), and higher than the mean for the preceding 5 years (22%). The early mortality rate was 10%, which is lower than the mean for the preceding 5 years (13%). After combining the results for 2004 with those of previous years, the probability of survival at 1, 5 and 10 years was 80%, 70%, and 60%, respectively. When the survival rates for different time periods were analyzed, a significant improvement could be seen in the last 5 years, with recent survival rates being 85% and 72% at 1 and 5 years, respectively. The most frequent cause of death in the first month was acute graft failure; in the first year, infection and rejection; and, over the long term, tumors and a combination of graft vasculopathy and sudden death. A comparative analysis of survival rates showed that long-term results in Spain are slightly better than those published in the world literature. Moreover, survival has tended to improve gradually in recent years.

Key words: Heart transplantation. Registry. Survival.

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En este artículo se describen las características generales y los resultados obtenidos con el trasplante cardíaco en España tras incluir los datos del último año. En 2004 se efectuaron 294 trasplantes que, junto con los realizados desde 1984, hacen un total de 4.680. El perfil clínico medio del paciente que se trasplanta en España corresponde a un varón de aproximadamente 50 años, de grupo sanguíneo A, con una enfermedad coronaria no revascularizable y en situación funcional IV/IV (NYHA).

El porcentaje de trasplantes cardiacos urgentes fue del 35%; esta cifra es muy superior a la del año previo (29%) y a la media de los últimos 5 años (22%). La mortalidad precoz fue del 10%, cifra inferior a la media de los últimos 5 años (13%).

Tras incorporar los resultados del pasado año a los previos se obtiene una probabilidad de supervivencia al primer, quinto y décimo años del 80, el 70 y el 60%, respectivamente. Al separar las curvas de supervivencia por períodos se aprecia la importante mejora en los últimos 5 años, con valores en el primer y quinto años del 85 y el 72%. La causa más frecuente de fallecimiento en el primer mes es el fallo agudo del injerto; en el primer año, la infección y el rechazo, y a largo plazo, los tumores y el combinado de enfermedad vascular del injerto con muerte súbita.

El análisis comparativo de la supervivencia muestra que los resultados a largo plazo son ligeramente superiores a los publicados en la bibliografía mundial, con una progresiva tendencia a mejorar la supervivencia en los últimos años.

Palabras clave: Trasplante cardíaco. Registro. Supervivencia.
INTRODUCTION

This article is the customary annual update analysis of results of heart transplantations performed in Spain between the first such procedure, performed in May 1984, and 31 December 2004.¹⁻¹⁵

This registry includes all heart transplants performed by all teams at all centers in Spain. 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 similar database constructed on mutually agreed principles, which unifies possible responses and standardizes variables.

HEART TRANSPLANTS PERFORMED

Eighteen heart transplantation centers supplied data for the registry (Table 1) although only 17 are actively performing transplants at present. Since 2001, the number of active centers in Spain has remained stable. Most transplantation teams believe there are too many centers and that it is unwise to increase their number as the benefit gained from shorter travel distances for patients is less than the inconvenience of the fact that new centers take a long time to gain the experience necessary to ensure good results.

In the 20 years that heart transplantation procedures have been being performed in Spain, the total number of operations has reached 4680. Figure 1 presents the distribution of the number of heart transplants per year. Of these, 96% were isolated orthotopic transplants. Table 2 shows the distribution of transplants by procedure type.

HEART TRANSPLANT RECIPIENT PROFILE AND BASELINE HEART DISEASE

In Spain, the profile of the average heart transplant recipient is that of a man of approximately 50 years of age with blood group A. Percentages of pediatric transplant recipients, older adults (>65 years) or women are rather low. Figure 2 presents the general characteristics of transplant recipients.

Heart transplantation is most frequently indicated for ischemic heart disease, followed by idiopathic dilated

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TABLE 1. Spanish Registry on Heart Transplantation, 1984-2004. Centers Reporting

1. Hospital Santa Creu i San Pau, Barcelona
2. Clínica Universitaria de Navarra, Pamplona
3. Clínica Puerta de Hierro, Madrid
4. Hospital Marqués de Valdecilla, Santander
5. Hospital Reina Sofía, Córdoba
6. Hospital La Fe, Valencia
7. Hospital Gregorio Marañón, Madrid
8. Fundación Jiménez Díaz, Madrid
9. Hospital Virgen del Rocío, Seville
10. Hospital 12 de Octubre, Madrid
11. Hospital Juan Canalejo, La Coruña
12. Hospital de Bellvitge, Barcelona
13. Hospital La Paz, Madrid
14. Hospital Central de Asturias, Oviedo
15. Hospital Clínic, Barcelona
16. Hospital Virgen de la Arrixaca, Murcia
17. Hospital Miguel Servet, Zaragoza
18. Hospital Clínico, Valladolid

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Figure 1. Number of heart transplants per year.

Together, these two diagnoses account for 76% of all causes. With the exception of valvular heart disease (9%), other specific causes are relatively infrequent. Figures 3 and 4 show the distribution of pathologic processes that are indications for heart transplantation.

WAITING LIST MORTALITY AND URGENT TRANSPLANTATION

In 2004, waiting list mortality was 9%. The percentage of patients excluded from transplant after placement on the waiting list was 16%. Figure 5 shows the annual percentages of waiting list patients who received a transplant, were removed from the list without receiving one, or died before receiving one.

Over the years, the percentage of indications for urgent transplantation has varied, sometimes substantially, often for no obvious reason. In 2004, urgent transplants accounted for 35% of procedures. This is a clear increase over 2003 (29%) and is above the average for the last 5 years (22%). Figure 6 shows the

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**Figure 2.** Annual distribution by age, blood group, and gender. Weight, height, and recipient functional status (weight and height excluding data on pediatric recipients). FS indicates functional status.

**Figure 3.** Baseline illness indicating transplantation and annual distribution. IHD indicates ischemic heart disease; IDCM, idiopathic dilated cardiomyopathy; Valv., valvular heart disease.

**Table 2.** Spanish Registry on Heart Transplantation, 1984-2004. Procedure Types

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthotopic heart transplants</td>
<td>4490</td>
</tr>
<tr>
<td>Heart retransplantations</td>
<td>97</td>
</tr>
<tr>
<td>Simultaneous transplantations</td>
<td></td>
</tr>
<tr>
<td>Heart-lung</td>
<td>53</td>
</tr>
<tr>
<td>Heart-kidney</td>
<td>34</td>
</tr>
<tr>
<td>Heart-liver</td>
<td>5</td>
</tr>
<tr>
<td>Heart-liver-pancreas</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>4680</td>
</tr>
</tbody>
</table>
evolution of indications for urgent transplantation over the years.

RESULTS

Survival

Early mortality (death ≤30 days post-transplantation) was 10% in 2004. Figure 7 shows the evolution of early mortality over the years.

When survival rate data for 2004 were added to those of previous years, we obtained 1-, 5-, and 10-year actuarial survival rates of 80%, 70%, and 60% respectively, with an average recipient survival of 13 years. Figure 8 shows the actuarial survival curve with an initially sharp decrease over the first year (essentially due to the first month) followed by a less marked decline of approximately 2.3% per year. Figure 9 shows that substantial differences exist when the overall survival curve is analyzed by periods.
The most frequent cause of death during the early period was acute graft failure (45%). Figure 10 shows the distribution of causes of death at ≤30 days.

The most common causes of overall mortality at >30 days were the combination of vascular graft disease and sudden death, acute graft failure and infection. Figures 11 and 12 show the incidence of causes of overall mortality.

When causes of mortality are distributed by periods, differences can be seen at ≤30 days (acute graft failure), 1 month to 1 year (infection) and >1 year (tumors and the combination of vascular graft disease with sudden death). Figure 13 shows the distribution of causes of mortality by periods.
DISCUSSION

In Spain, the early days of heart transplantation are long gone and today we can call on a wealth of experience with this procedure. Our results are on a par with those achieved in other countries both in Europe and around the world, as any analysis of the annual report of the Registry of the International Society for Heart and Lung Transplantation reveals.\textsuperscript{16-18}

Our Registry comprises information provided by all Spanish transplant teams and is founded on an agreed, standardized database which reinforces the validity of these results. All teams update results annually and submit figures to the Registry coordinator who, using custom-built software, introduces the data into a common database for subsequent analysis of variables. We believe this method greatly enhances the reliability of our results and avoids errors of the kind so often found in non-standardized databases.

In 2004, the number of active transplantation centers in Spain remained stable. We believe this is positive although it still causes concern among most teams because the number of optimal donors has remained constant whereas the relationship to transplantations and centers has decreased. The fact that fewer transplant procedures are being performed leads to underuse of resources in hospitals equipped to undertake a greater number of transplants and to the risk entailed in the long 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.

Since heart transplantation began in Spain, the number of procedures per year has increased steadily.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure10.png}
\caption{Causes of early mortality. AGF indicates acute graft failure.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure11.png}
\caption{Causes of overall mortality. SD+VGD indicates sudden death and vascular graft disease; AGF, acute graft failure.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure12.png}
\caption{Less frequent causes of overall mortality. The number to the end of each of the columns represents percentage with respect to the total. AGF indicates acute graft failure.}
\end{figure}
The period 1989-1993 saw the greatest increase in transplantations with the number of procedures rising from 97 to 287 per year. Since 1993, the rate of increase has fallen and 2000 was the only year to surpass 350 transplantations. Considered at the time a probable plateau, this figure seems excessively high as in the last three years procedures have stabilized at around 300 per year, despite an increase in the upper age limit for donors.

The future of simultaneous heart-lung transplants is still unclear and this procedure has yet to become firmly established. Few teams perform heart-lung transplants and few procedures are carried out each year. In 2004, only 7 operations of this kind were performed in Spain and such a high number of procedures had not been recorded since 1998. The development of this type of transplant is complicated by the technical difficulties involved, the so-called “consumption” of organs and the substantially worse prognosis associated with it by comparison with separate heart and lung transplantation. Of the other simultaneous transplantations, heart-kidney procedures are the most advanced (34 procedures in total) with a clearly better prognosis than heart-lung transplantations.

For some years, ischemic heart disease has been the most frequent indication for heart transplantation in Spain. This is not surprising given the prevalence of the disease in the country. In some international registry reports the most frequent cause is dilated cardiomyopathy but this may be a terminologic issue as ischemic heart disease accompanied by substantial ventricular dilation is defined as dilated cardiomyopathy.

The importance of waiting list mortality may be underestimated as it only considers patients who die while on the list, ignoring those removed due to severe decompensation with multiple organ failure who die after removal from the list. In 2004, the number of patients who died and the number who were excluded from the waiting list were 9% and 16%, respectively.

Urgent heart transplantations are controversial as they are operations with specific characteristics (recipients in worse clinical condition, often less-than-ideal donors, longer periods of ischemia) that entail a worse prognosis than programmed transplants. In 2004, the percentage of urgent transplants increased substantially again (35% in 2004 vs 29% in 2003) and represented an increase over the mean for the last 5 years (22%). Although urgent procedures imply greater risk, transplant teams believe they should continue to be performed given they are the only option open to the subgroup of patients with advanced heart failure and uncontrollable acute decompensation. However, as European guidelines on acute heart failure recommend, it is probably better to stabilize heart failure rather than indicate for urgent transplantation.

Over the years, overall survival has tended to improve progressively. However, the number of patients added to the Registry each year represents a comparatively smaller percentage of the total. Thus, the chances of finding substantial changes within a single year are very remote and analysis of survival by eras is more illuminating.

When evaluating this Registry and comparing it with others we must remember that it includes all transplantation procedures and reliably portrays the reality of transplantation in Spain. However, analyses are global and also include high risk transplantations (urgent transplants, older age group recipients, pediatric transplants, retransplants, heterotopic transplantations, combined heart-lung, heart-kidney, heart-liver and other simultaneous transplantations).

In 2004, early mortality (death ≤30 days) was 10%, which was lower than the mean for the last 5 years.
The most frequent cause of early mortality was acute graft failure which accounts for 45% of mortality during this period. Despite being a postoperative problem, the impact of acute graft failure is so great that it causes a substantial number of deaths (19%) at >1 month too. Note that mortality due to rejection (early mortality 7%, late mortality 9%) is somewhat less than that caused by infections (early mortality 14%, late mortality 18%). Perhaps transplant teams should consider reducing immunosuppression regimens even though it might lead to a higher number of rejection episodes.

To conclude, we can say that:

1. In recent years, the annual volume of heart transplantations has fallen despite the gradual inclusion of older donors. The number of procedures seems to have stabilized at around 300 per year.
2. Heart-lung transplantation has not yet become firmly established in Spain. There are few such transplantations each year.
3. In general (early and late) survival rate figures are above those published in many international registry reports and have improved yearly, especially in the last 5 years.
4. We should continue to try to reduce the high incidence of acute graft failure. This would have a substantial positive effect on the probability of immediate post-operative and overall survival.

REFERENCES