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Heart transplantation in Spain: a review of the heart transplant programme in Spain from its beginning in 1984 by Marisa Crespo-Leiro MD

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Heart transplantation (HT) was first performed in Spain in 1984. By the end of December 2016, 7869 HTs had been performed in 19 centres (*Table 1*). One of these centres ceased HT activity in 1994, and of the remaining 18, 2 perform HT exclusively on paediatric patients, i.e. those younger than 16 years, 12 exclusively on adults, and 4 on both adult and paediatric patients.

Table 1. Centres participating in the Spanish Heart Transplant Registry (1984–2016), listed by order of date of their first transplantation

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1. Hospital de la Santa Creu i Sant Pau, Barcelona
 2. Clínica Universitaria de Navarra, Pamplona
 3. Clínica Puerta de Hierro, Majadahonda, Madrid
 4. Hospital Marqués de Valdecilla, Santander
 5. Hospital Reina Sofía, Córdoba (adult and paediatric)
 6. Hospital Universitario y Politécnico La Fe, Valencia (adult and paediatric)
 7. Hospital Gregorio Marañón, Madrid (adult and paediatric)
 8. Fundación Jimenéz Díaz, Madrid (1989-1994)
 9. Hospital Virgen del Rocío, Seville
 10. Hospital 12 de Octubre, Madrid
 11. Hospital Universitario de A Coruña, La Cornña (adult and paediatric)
 12. Hospital Bellvitge, L'Hospitalet de Llobregat, Barcelona
 13. Hospital La Paz, Madrid (paediatric)
 14. Hospital Central de Asturias, Oviedo
 15. Hospital Clínic, Barcelona
 16. Hospital virgin de la Arrixaca, El Palmar, Murcia
 17. Hospital Miguel Servet, Zaragoza
 18. Hospital Clínico, Valladolid
 19. Hospital Vall d'Hebron, Barcelona (paediatric)
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In 2016, 261 adult and 20 paediatric HTs were performed, their distribution among the 18 centres summarized as 10 or fewer in 5 centres, 11–20 in 10, and more than 20 in 3 centres.

The Spanish Heart Transplant Registry

The Spanish Heart Transplant Registry archives data on all HTs performed in Spain since the programme started in 1984. Since 1991 *Revista Española de Cardiología* has published an annual analysis of these data (the figures reported in this article are taken from the 28th report, available at <http://www.revespcardiol.org/es/registro-espanol-trasplante-cardiaco-xxviii/avance-resumen/S0300893217305146/>).

Over the years, the information documented in the registry has become progressively more detailed and it now records for each HT 175 variables characterizing recipients, donors, surgical techniques, immunosuppression and follow-up. Since 2013 when web-based on-line data input was initiated, it has included data formerly deposited in the Spanish Post-HT Tumour Registry, which was set up in 2003 with the primary objective of improving our knowledge of the incidence, risk factors and natural history of post-HT neoplasms with a view to the identification of areas for improvement.

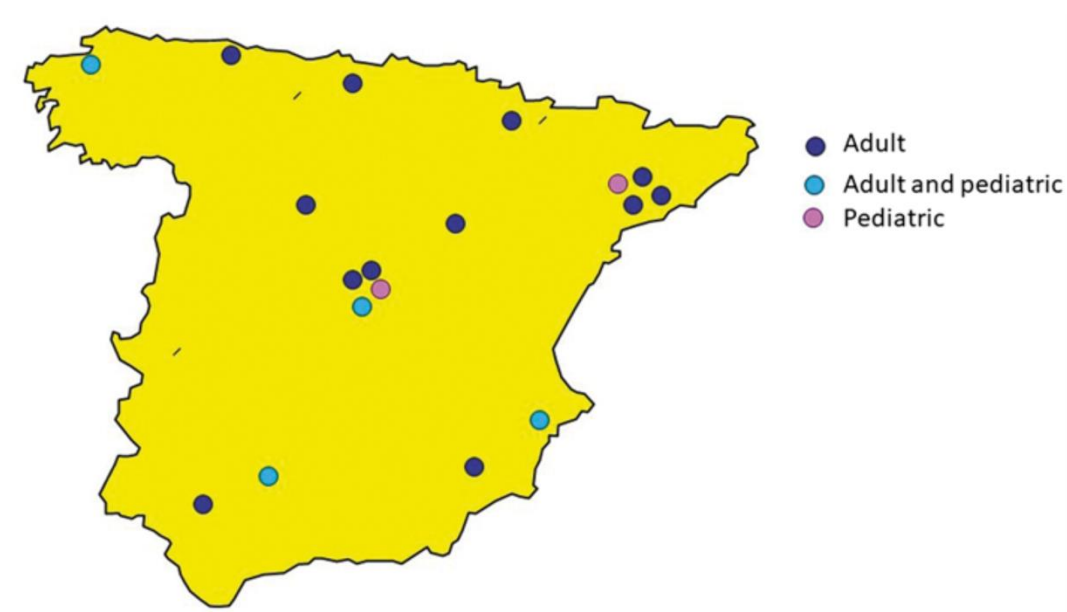


Figure 1. Geographical distribution of heart transplant centres in Spain 2017.

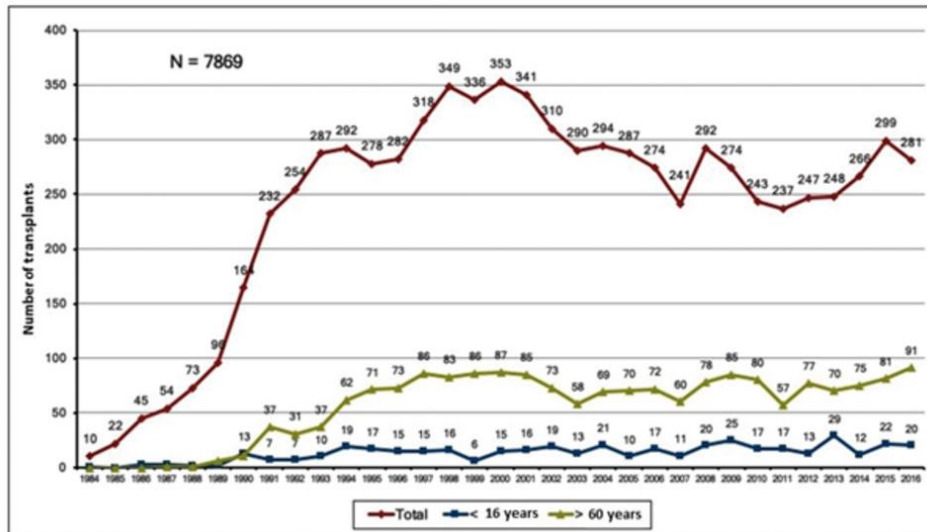


Figure 2. Annual heart transplant procedures in Spain (1984–2016).

Therefore, it now includes information on issues such as pre-HT risk factors for tumours, the course of immunosuppression, infections, the use of antivirals, post-HT tumours (coded as per SNOMED in terms of location and pathology), stage at diagnosis, and the treatment and evolution of the tumour. Spanish data protection legislation (Organic Law 15/1999) complies with an ethics committee approval, auditing, and registration with the Ministry of Health.

Donation

In 2016, the number of organ donors in Spain was 43.4 per million population (pmp), allowing more than 100 transplant procedures pmp. Thus, Spain remains a world leader in the provision of transplants of all kinds, despite the number of healthy young donors having fallen because of a welcome reduction in the number of traffic fatalities. The reduction in this source of donors is reflected in the number of HTs performed annually, which fell from a peak of 353 in 2000 to 241 in 2007. To offset this fall in optimal donors, the Spanish National Transplantation Organization and Heart Transplant Teams have progressively adopted more flexible criteria for organ selection, particularly regarding the use of older donors; in 2016, 57% of heart donors were older than 45 years (*cf.* 7.6% for the period 1993–1984 period, 19.3% for 1994–2003, and 35.6% for 2004–2013). As a result of this and other measures, the annual HT rate has recovered over the past decade, reaching 299 in 2015. The 2016 figure of 281 equals 6.5 pmp (the figure of 6.1 pmp reported by the Global Observatory on Donation and Transplantation fails to take into account the drop in the Spanish population in recent years). The change in the characteristics of the typical heart donor is also apparent in their cause of death: in 2016, 56.4% died of stroke and only 27% from trauma (*cf.* 31.8% for stroke and 63.5% for trauma in the period 1984–1993). Ischaemic time was greater than 4 h in 27% of donations (*cf.* 8.7% in 1984–1993).

Patient prioritization

Every year the criteria for patient prioritization for the reception of a heart graft are revised by consensus at a meeting attended by representatives of the Spanish National Transplantation Organization and of all 18 heart transplant centres. From 2010 to 2016, patients were assigned to one of the three priority levels: urgency status 0, urgency status 1, and elective.

The highest priority, urgency status 0, was reserved for HT candidates who are dependent on temporary mechanical circulatory support (MCS) and cannot be weaned off the device, or those with durable ventricular assist devices (VADs) who have developed complications such as infection, pump failure, or thrombosis; the scope of urgency status 0 is nationwide, i.e. a patient with this status anywhere in Spain takes priority over all patients with lower status.

Urgency status 1 was assigned to patients in cardiogenic shock requiring (i) vasoactive drugs and invasive mechanical ventilation, and/or (ii) intra-aortic balloon pumping, and/or (iii) long-term VAD; and to patients in arrhythmic storm (for paediatric patients there are also some other conditions leading to urgency status 1). A patient with urgency status 1 takes priority over those with elective status within the catchment area of his or her centre. Patients not satisfying any of the above-mentioned criteria were assigned elective status.

As an example of how the criteria are redefined every year, in 2017 one of the criteria for 'urgency 0', was modified. Thus, patients with extracorporeal membrane oxygenation (ECMO) or any temporary MCS offering partial support, must be on the MCS a minimum of 48 h before entering the urgency status 0 list and only provided they do not present criteria of multi-organ failure. The maximum time of stay for these patients in urgency grade 0 is limited to 7 days. After that time from inclusion in urgency 0 status, the patient will go to grade 1 urgency.

The death rate on the waiting list is low, oscillating in the range 3.2–4.4% in recent years.

Recipients and results

In 2016, recipients were on average aged 50 years, 75% were male, and the main underlying diagnoses were ischaemic cardiomyopathy and non-ischaemic dilated cardiomyopathy. Although the mean patient age has remained very stable over the years, there has been a significant increasing trend in the age of both recipients older than 60 years and paediatric recipients. Concerning recipients over 60 years there has also been an increase in the proportion of patients with pre-transplant conditions with an adverse effect on post-transplant prognosis: in 2016, 22% of patients had insulin-dependent diabetes, 29% had undergone previous cardiac surgery and while awaiting transplant 20% had suffered a relevant infection and another 17% had required mechanical ventilation. Over 50% of recipients were in urgency status 0 or 1.

Regarding therapeutic trends, in 2016 continuous flow VADs were used by 45% of recipients requiring pre-HT mechanical circulatory support. Over 80% received induction therapy, and in the first-year post-HT over 90% used tacrolimus as a calcineurin inhibitor, over 97% mycophenolate mofetil as an anti-proliferative agent, and 99% a steroid. During the whole period 1984–2016, 30% of patients were taking an mTOR inhibitor at their last or latest follow-up visit, and 64% a steroid.

The Kaplan–Meier survival has improved steadily over the years. Following the improvement in survival during the first-year post-HT that occurred about 1990, long-term survival has also shown improvement. In the period 2004–2013, 1 year of survival was approximately 77% and 10 year of survival about 58%; and figures shows that the data for 2014–2016, though inconclusive because of the small population, appear to indicate a further increase in survival.

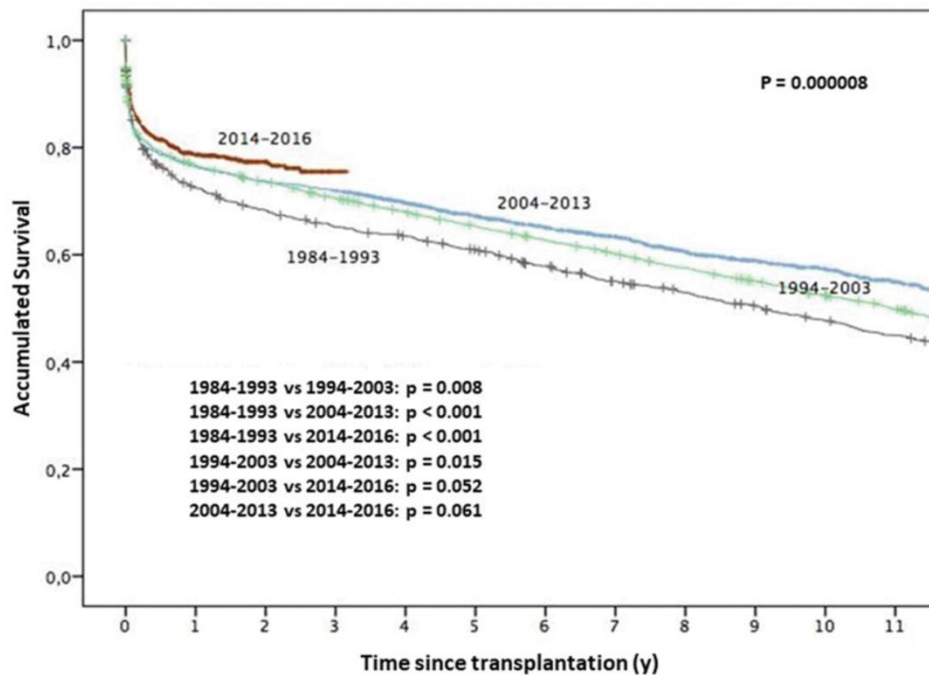


Figure 3. Survival after heart transplantation in Spain by eras.

Networking and research

The efficiency of the Spanish transplantation system is based on close between-group coordination and collaboration. In the case of HT, these ties are furthered by two annual meetings, among other events. One of these meetings, mentioned above, is convened at the beginning of each year by the National Transplantation Organization for review of the criteria for patient prioritization, organ distribution and related issues, and for presentation and discussion of the statistics of the previous year. This meeting is attended by at least two representatives of each transplantation centre (the surgical and medical director of each HT programme) and by transplant coordinators. The other major event is the annual meeting of the Heart Failure Section of the Spanish Society of Cardiology, at which a session is devoted to the presentation, by each transplant centre, of the epidemiological and clinical details of the HTs performed in that centre during the previous year, including discussion of challenging cases in which decision-making is difficult.

The links forged over the years between HT teams have also been fundamental in the design and execution of several research projects and related initiatives. In the first place, they have allowed the establishment and maintenance of the Spanish Heart Transplant Registry (which contributes to the Registry of the International Society for Heart and Lung Transplantation) and the Post-HT Tumour Registry, which have been and continue to be valued sources of much useful information. They have also facilitated research initiatives such as the SIMCOR trial, which compared baxilisimab with muromonab after HT; CAPRI, a cross-sectional study of renal dysfunction after HT; RESTCO, a study of steroid withdrawal after HT; ASIS-TC, a study of temporary mechanical circulatory support for urgent transplantation candidates, the results of which have recently been published; as well as numerous nameless studies that have investigated, for example, HT outcomes with donors older than 50 years, HT outcomes using different immunosuppression protocols (example: use of mTOR inhibitors or tacrolimus extended-release), HT outcomes by CMV infections or the usefulness of the INTERMACS profile for predicting outcomes after urgent HT.

In summary, because the number of HTs per year, at any single centre in Spain is necessarily low, networking among centres is of singular value to the heart transplant programs in Spain and it should be further intensified to allow us to respond to relevant clinical questions in the field; amongst others, the optimal and equitable organ allocation throughout Spain in a situation of chronic organ shortage.