Special article

Spanish heart transplant registry. 34th official report of the Heart Failure Association of the Spanish Society of Cardiology



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ABSTRACT

Introduction and objectives: The Spanish heart transplant registry updates its data annually. The current update presents the data for the year 2022.

Methods: We describe the main clinical characteristics, treatments received, and survival outcomes including procedures performed in 2022, along with their trends since 2013.

Results: In 2022, 311 cardiac transplants were performed, representing a 3.0% increase compared with 2021. Compared with previous years, no significant changes in demographic and clinical characteristics were observed in 2022, confirming the trends identified in the last decade. These trends indicate a decrease in urgent procedures and the use of circulatory support, particularly ventricular assist devices. In the last decade, survival rates at 1 and 3 years were 81.4% and 73.4% respectively, with a slight, nonsignificant improvement.

Conclusions: In the last decade, there has been a stabilization in the characteristics of heart transplant procedures and their outcomes.

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Registro español de trasplante cardiaco. XXXIV informe oficial de la Asociación de Insuficiencia Cardiaca de la Sociedad Española de Cardiología

RESUMEN

Introducción y objetivos: El Registro español de trasplante cardiaco actualiza sus datos anualmente. En este artículo se presentan los datos correspondientes al año 2022.

Métodos: Se describen las principales características clínicas, del tratamiento recibido y de los resultados en términos de supervivencia de los procedimientos realizados en 2022, así como las tendencias de estos desde el año 2013.

Resultados: En 2022 se han realizado 311 trasplantes cardiacos (un 3,0% más que el año anterior). No se han observado cambios relevantes en las características demográficas y clínicas en 2022 respecto a los años inmediatamente anteriores, lo que confirma las tendencias ya descritas en la última década a una

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disminución de los procedimientos urgentes y el uso de asistencia circulatoria, sobre todo de dispositivos de asistencia ventricular. En el último decenio, las supervivencias son del 81,4 y el 73,4% a 1 año y a los 3 años, con una mejoría numérica que no ha alcanzado significación estadística.

Conclusiones: En la última década se observa una estabilización en las características de los procedimientos de trasplante cardiaco y de sus resultados.

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INTRODUCTION

The heart transplant field can consider 2022 to be the first year that was completely free of the effects of the SARS-CoV-2 pandemic. A constrained influence of the pandemic on both activity and mortality outcomes was detected in previous reports of the Spanish heart transplant registry.¹ The present report includes information on the procedures performed in 2022 and updates the historic series, particularly regarding mortality data. As is tradition, the main findings are centered on procedures performed in the last 10 years (2013-2022).

METHODS

Patients and procedures

The current report provides data on transplants performed in 2022. In addition, we have analyzed the changes over time in the characteristics of the series in the previous decade, stratified by 3-year periods (2013-2015, 2016-2019, and 2020-2021). The percentages of some characteristics in the last decade were analyzed by year, such as urgent transplants, type of pretransplant circulatory support, and donor age.

Table 1

Centers participating in the Spanish heart transplant registry from 1984 to 2022 (by order of first transplant performed)

1.	Hospital de la Santa Creu i Sant Pau, Barcelona
2.	Clínica Universidad de Navarra, Pamplona, Navarra
3.	Hospital Universitario Puerta de Hierro-Majadahonda (adult, cardiopulmonary), Majadahonda, Madrid
4.	Hospital Universitario Marqués de Valdecilla, Santander, Cantabria
5.	Hospital Reina Sofía (adult and pediatric), Córdoba
6.	Hospital Universitario y Politécnico La Fe (adult and pediatric, cardiopulmonary), Valencia
7.	Hospital General Universitario Gregorio Marañón (adult and pediatric), Madrid
8.	Hospital Universitario Fundación Jiménez Díaz, Madrid (1989- 1994)
9.	Hospital Universitario Virgen del Rocío, Seville
10.	Hospital Universitario 12 de Octubre, Madrid
11.	Complexo Hospitalario Universitario A Coruña (adult and pediatric), A Coruña
12.	Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona
13.	Hospital Universitario La Paz, Madrid (adult and pediatric)
14.	Hospital Universitario Central de Asturias, Oviedo, Asturias
15.	Hospital Clínic de Barcelona, Barcelona
16.	Hospital Clínico Universitario Virgen de la Arrixaca, El Palmar, Murcia
17.	Hospital Universitario Miguel Servet, Zaragoza
18.	Hospital Clínico Universitario de Valladolid, Valladolid
19.	Hospital Universitari Vall d'Hebron (pediatric), Barcelona
20.	Hospital Universitario de Gran Canaria Doctor Negrín, Las Palmas de Gran Canaria

The inclusion and data updating procedures of the Spanish heart transplant registry have not undergone major changes from previous years.² Crucially, the Spanish heart transplant registry was established as a registry of procedures (transplants performed), not of patients. Accordingly, a retransplanted patient generates 2 distinct records that are analyzed separately. Participation in the Spanish heart transplant registry is voluntary for all transplant teams operating in Spain. In a change from previous years, Hospital Universitario La Paz (Madrid) started in 2022 to include adult patients (age at transplant \geq 18 years) undergoing transplants for congenital heart disease. Accordingly, the registry shows the same number of Spanish transplant centers, even though only 1 of these centers now performs pediatric transplants alone (table 1).

The total numbers and types of transplant performed in 2022 and in the entire series are summarized in table 2. In 2022, 311 transplants were performed; most (n = 300) were de novo heart transplants. Thus, 9 retransplants (2.9%) were performed, as well as 1 combined heart-kidney transplant and 4 combined transplants (2 de novo heart-kidney transplant, 1 de novo heart-liver transplant, and 1 heart-kidney retransplant). By age, 28.9% of recipients (90 transplants) were older than 60 years and 11.6% (n = 36) were younger than 18 years. Overall, the Spanish heart transplant registry has recorded 9673 procedures (figure 1).

Statistical analysis

Continuous variables are expressed as mean \pm standard deviation, whereas categorical variables are expressed as percentages. Differences among time periods were analyzed using a nonparametric test for temporal trends (Kendall τ) for categorical variables and a Wilcoxon test for trends for continuous variables.³ Survival curves were calculated using the Kaplan-Meier method and were compared using a log-rank test. Differences were considered statistically significant at *P* < .05.

RESULTS

Recipient characteristics

In 2022, 311 transplants were performed, 9(3.0%) more than in the previous year, which stabilizes the number of procedures

Table 2

Spanish heart transplant registry (1984-2022). Type of procedure

Procedure	2022	1984-2022
De novo heart transplant	300	9266
Heart retransplant alone	8	217
Combined heart retransplant	1*	8*
Combined de novo heart transplant	3	183
Heart-lung	0	89
Heart-kidney	2	78
Heart-liver	1	16
Total	311	9673

* All kidney transplants.



Figure 1. Annual number of transplants (1984-2022), total and by age group.

performed at about 300 per year (figure 1). The main recipient characteristics in 2022 and from 2013 to 2022 are summarized in table 3. In the overall population, the mean recipient age has shown no significant changes in the last 10 years and remains 49.0

years (48.0 years in 2022). Similar stability was observed in recipients \geq 18 years at transplant (53.2 years in the last decade, 53.3 years in 2022). There was a nonsignificant tendency for a higher proportion of female recipients in the last decade, which

Table 3

Recipient characteristics in the Spanish heart transplant registry (2013-2022)

Characteristics	2013-2015 (n=813)	2016-2018 (n=906)	2019-2021 (n=880)	P for trend	2022 (n=311)
Age, y	48.8 ± 17.1	49.2 ± 17.7	49.3 ± 17.3	.37	48.0 ± 18.6
<18 y	8.6	9.5	8.6	.86	11.6
>60 y	27.8	30.1	29.3	.34	28.9
Male sex	74.4	72.5	70.5	.19	71.1
BMI	24.5 ± 4.5	24.7 ± 4.8	$\textbf{24.7} \pm \textbf{4.8}$.34	24.9 ± 9.4
Underlying etiology				.42	
Nonischemic dilated	34.6	36.6	35.6		32.2
Ischemic	36.6	32.7	31.7		33.1
Other	28.8	30.7	32.7		34.7
PVR, WU	2.2 ± 1.2	2.2 ± 1.3	2.0 ± 1.3	<.01	2.0 ± 1.1
Glomerular filtration rate, mL/min/1.73 m ²	79.6 ± 33.5	$\textbf{80.3} \pm \textbf{34.4}$	$\textbf{79.9} \pm \textbf{35.4}$.69	81.0 ± 40.6
Bilirubin > 2 mg/dL	16.2	16.8	12.1	.08	9.6
Insulin-dependent diabetes	22.2	21.1	19.5	.09	21.5
Moderate-severe COPD	11.8	10.5	9.3	.26	5.7
Previous infection	14.5	16.0	14.5	.92	19.2
Previous cardiac surgery	37.2	45.2	47.1	<.001	43.6
Type of transplant				.69	
Isolated	96.6	96.4	96.3		96.5
Heart retransplant	1.9	1.6	1.8		2.6
Combined	1.6	2.1	1.9		0.9
Heart-lung	0.8	1.0	0.5		0
Heart-kidney	0.7	0.4	0.7		0.6
Heart-liver	0	0.2	0.3		0.3
Pretransplant mechanical ventilation	15.2	14.5	13.6	.64	9.9
Urgent transplant	45.9	46.8	38.4	.14	37.6
Pretransplant circulatory support				<.01	
No	62.0	58.2	63.3		64.8
Balloon pump	13.7	4.1	1.4		0.7
ЕСМО	11.2	10.5	8.0		8.1
Ventricular support	12.2	27.2	27.4		26.4

BMI, body mass index; COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation; PVR, pulmonary vascular resistance. Values are expressed as percentage or mean ± standard deviation.





Figure 3. Distribution of the type of pretransplant circulatory support by year (2013-2022). ECMO, extracorporeal membrane oxygenation; VAD, ventricular assist device.

reached 28.9% in 2022. Similarly, a tendency was detected for improved clinical status among recipients, as well as for a lower proportion of patients with diabetes or with elevated bilirubin at transplant. This tendency was significant for pulmonary vascular resistance, which has decreased up to 2.0 Wood units, a finding maintained in 2022. The trend was confirmed in 2022 for a lower percentage of urgent transplants (37.6%), and the difference was significant compared with 2013 (P < .001) (figure 2). Since 2019, this percentage has consistently been less than 40%. The data from 2022 confirmed the highly significant temporal trends in the distribution of the type of immediate pretransplant circulatory support devices used (figure 3). In the last 5-year period, 562 patients (37.8% of the total number of patients transplanted in this period) were transplanted with some type of circulatory assist device. Most of these devices were continuous-flow ventricular assist devices (367 patients; 24.7% of all recipients), followed by extracorporeal membrane oxygenation (ECMO) devices (133 patients; 8.9%) and pulsatile ventricular assist devices (46 patients; 3.1%). The maginal use of balloon pump (16 patients;

1.1%) was maintained during this period. In 2022, these percentages largely matched those of the last 5-year period.

Donor and surgical procedure characteristics

Donor and surgical procedure characteristics are summarized in table 4. Donor age has remained stable in the last decade (figure 4), at an average of 42.5 ± 15.2 years in the last 10 years (41.1 ± 16.3 years in 2022). Similar stability was seen for the percentage of suboptimal donors, that is, donors older than 45 years old, which has been 52.2% on average in the last decade (49.5% in 2022). At least until 2021, the only statistically significant characteristic was the use of larger donors (*P* for trend = .04), although this has not resulted in a particularly unfavorable donorto-recipient weight ratio (> 1.2 or < 0.8).

The most pertinent data regarding the donation process, which were consolidated in 2022, were donation after circulatory death (asystole) and ABO-incompatible transplantation. Donation after

Table 4

Donor characteristics and procedure times in the Spanish heart transplant registry (2013-2022)

Characteristics	2013-2015 (n=813)	2016-2018 (n=906)	2019-2021 (n=880)	P for trend	2022 (n=311)
Age, y	42.4 ± 14.6	43.4 ± 15.5	42.2 ± 15.2	.91	41.1 ± 16.3
>45 y	50.1	57.2	49.9	.4	49.5
Male sex	57.3	60.9	60.3	.13	66.9
Female donor-male recipient	26.1	22.1	20.5	.02	14.2
Weight, kg	73.3 ± 18.8	74.3 ± 19.2	74.6 ± 19.7	.04	73.7 ± 21.0
Recipient/donor weight	0.93 ± 0.19	$\textbf{0.93} \pm \textbf{0.20}$	$\textbf{0.93} \pm \textbf{0.19}$.37	$\textbf{0.93} \pm \textbf{0.22}$
Recipient/donor weight > 1.2	7.9	8.7	6.8	.53	9.3
Recipient/donor weight < 0.8	21.7	23.7	24.4	.13	24.1
Cause of death				.82	
Trauma	24.1	21.2	21.7		24.4
Stroke	62.0	63.3	64.8		55.0
Other	13.9	15.7	13.5		20.6
Pretransplant cardiac arrest ^a	17.2	17.4	19.5	.21	31.0
Predonation echocardiogram ^b				.88	
Not performed	1.3	1.8	0.4		0
Normal	95.5	95.4	97.7		97.3
Mild generalized dysfunction	3.2	2.8	1.9		2.7
Ischemia time	203.0 ± 66.9	197.2 ± 71.3	195.2 ± 72.7	<.01	188.1 ± 72.2
≤ 120 min	12.4	17.8	17.3	.03	20.9
120-180 min	22.5	19.9	23.2		25.1
180-240 min	38.3	34.7	35.3		30.2
>240 min	26.8	27.7	24.2		23.8
Bicaval surgical technique	67.5	72.3	76.0	<.001	83.1

Values are expressed as percentage or mean \pm standard deviation.

^a Of 2406 transplants.

^b Of 2237 transplants.

circulatory death was performed in 52 patients in 9 centers (4 patients in 2020, 11 in 2021, and 37 in 2022). In addition, 15 ABO-incompatible transplants were performed from 2018 to 2022, all in pediatric patients (4 in 2018, 2 in 2019, 2 in 2020, 4 in 2021, and 3 in 2022).

As seen in previous reports, the mean ischemia time has significantly decreased in the last 10 years (table 4) and was slightly longer than 3 hours in 2022. This decrease was largely due to an increase in the number of procedures performed with an

ischemia time less than 2 hours. We continue to see significant growth in the bicaval technique, used in more than 80% of patients in 2022.

Immunosuppression

Table 5 summarizes the trends related to the drugs used for induction immunosuppression. Data similar to those of the most



Figure 4. Annual changes in donor age and the percentage of donors older than 45 years (2013-2022). 95% CI, 95% confidence interval.

Table 5

Induction immunosuppression in the Spanish heart transplant registry (2013-2022)

Immunosuppressant	2013-2015 (n=813)	2016-2018 (n=906)	2019-2021 (n=880)	P for trend	2022 (n=311)
Calcineurin inhibitors		1		<.001	
Cyclosporin	12	5.3	3.7		1.0
Tacrolimus	88	94.7	96.3		99.0
Antiproliferative agents				.86	
Mycophenolate mofetil/mycophenolic acid	99.1	99.0	99.4		99.7
Azathioprine	0.9	1	0.6		0.3
mTOR inhibitors					
Sirolimus	0.3	0.6	0.3	>.999	0.4
Everolimus	2.1	1.3	0.9	.05	1.6
Steroids	97.1	97.1	97.9	.34	99.0
Induction				<.001	
No	13.8	17.1	17.0		21.1
ALG/ATG	2.7	4.3	3.6		3.8
Anti-CD25	83.2	77.4	79.3		79.2
Other	0.4	1.2	0.1		0.5

ALG, antilymphocyte globulin; anti-CD25, basiliximab, daclizumab; ATG, antithymocyte globulin.

Values are expressed as percentages.

recent years were obtained in 2022, although significant tendencies can still be detected when the comparison is extended to the beginning of the previous decade. Induction with anti-CD25 (currently only performed with basiliximab) and triple therapy with tacrolimus, mycophenolate mofetil (or mycophenolic acid), and steroids form the basis of the induction immunosuppressive therapy in the overwhelming majority of patients.

Survival

Survival in the 2013 to 2022 period was 81.4% in the first posttransplant year and 73.4% at 5 years. This rate is significantly higher than that seen in the entire historic series (figure 5A). No significant improvement in survival was detected in the last decade (figure 5B). However, numerically, 1-year survival has constantly improved: 79.7% from 2013 to 2015, 81.7% from 2016 to 2018, and 82.2% from 2019 to 2021. Some of the univariable predictors of mortality are summarized in table 6. The factors most strongly associated with mortality were those related to the recipient's pretransplant clinical status (need for advanced circulatory support or mechanical ventilation) and to comorbidity (age, pretransplant infection, diabetes or pretransplant renal failure, ischemic etiology).

Causes of death

The specific causes of death in the first 5 posttransplant years were primary graft failure (23.2%) and infection (21.0%) (figure 6). As expected, the main causes of death were primary graft failure in the first posttransplant month (39.3%) but infection between 2 and 12 months (44.9%). Acute rejection was the cause of death in 7.1% of patients between the 2nd and 12th posttransplant months. Although rejection was the fourth cause of death in the first 5 posttransplant years, its prevalence was not negligible after the first year (14.6% of patients). After the first posttransplant year, the most frequent causes of death were graft vascular disease/sudden cardiac death (23.8%) and cancer (19.5%).



Figure 5. A: comparison of survival curves between the 2013 to 2022 and 1984 to 2012 periods. B: comparison of survival curves from 2013 to 2021 by 3-year period.

Table 6

Univariable analysis of survival by baseline characteristics of the recipient, donor, and procedure (2013-2022)

Variable	Hazard ratio (95%CI)	Р
Recipient age		
<18 y	1	
18-60 y	1.3 (1.0-1.8)	.05
>60 y	2.0 (1.5-2.8)	<.001
Underlying etiology		
Nonischemic dilated	1	
Ischemic dilated	1.4 (1.2-1.6)	<.001
Other	1.2 (1.0-1.4)	.09
Type of transplant		
Isolated heart transplant	1	
Combined transplant	1.6 (1.0 -2.3)	.07
Retransplant	1.2 (0.7-2.0)	.48
Donor age		
≤ 45 y	1	
>45 y	1.1 (0.9-1.3)	.07
Urgency code		
Elective	1	
Urgent	1.3 (1.1-1.5)	<.001
Type of support		
No support	1	
Balloon pump	0.9 (0.7-1.2)	.51
ECMO	1.7 (1.4-2.1)	<.001
Ventricular support	1.3 (1.1-1.5)	<.001
Pretransplant creatinine $> 2 \text{ mg/dL}$	1.5 (1.3-1.7)	<.001
Pretransplant mechanical ventilation	1.9 (1.6-2.2)	<.001
Pretransplant infection	1.5 (1.2-1.8)	<.001
Pretransplant diabetes	1.3 (1.1-1.5)	<.001

95%CI, 95% confidence interval; ECMO, extracorporeal membrane oxygenation.

The last decade has shown a significant decrease in rejection as the cause of death in the first year (from 7.3% from 2013 to 2015 to 2.6% from 2019 to 2021), although an uptick was detected in 2022 (4.2% of all deaths). However, the prevalences of primary graft

failure and infections as causes of death have remained stable in the last 10 years (figure 7).

DISCUSSION

From the perspective offered by the sustained effort of the Spanish heart transplant registry, analysis of the temporal trends in recent years appears to show the stability of heart transplantation activity in Spain regarding the characteristics of recipients, donors, surgical procedures, and immunosuppressive therapy. In this regard, the prototypic patient in Spain in recent years has been a man in 3 of every 4 cases, aged about 50 years and who, in slightly more than one third of cases, undergoes an urgent transplant. typically with a ventricular assist device. The transplant was performed in half of the cases with a donor who would conventionally be considered suboptimal. In addition, we may be seeing signs of effort to more strictly select recipients with a better risk profile (tendency for fewer recipients with pretransplant diabetes) and better general status immediately before transplant (improved bilirubin values and fewer and fewer patients on mechanical ventilation every year). Notably, the efforts of the organ procurement system and surgical teams have resulted in progressively shorter ischemia times and extensive use of the bicaval technique. No major novelties have been seen in relation to immunosuppressants, and most patients are induced with basiliximab and almost all receive triple therapy based on tacrolimus, mycophenolate mofetil, and steroids. In this general framework, the survival outcomes can be considered equivalent to those of other international registries.⁴ The 1-year survival exceeds 80% and three quarters of patients are still alive at 5 years, with the median survival of transplant recipients exceeding 12 years in the last decade.

Currently, ongoing work within the heart transplant field is aimed at improving the balance between procedure availability and futility and at increasing the supply of donors. The first aspect includes the recent modification of the organ allocation criteria of the Spanish National Transplant Organization,⁵ in which the analysis provided by the Spanish heart transplant registry played a decisive role. The second aspect includes ABO-incompatible transplantation, a technique that is being adopted worldwide and ever more frequently in Spain⁶ and that constitutes an opportunity to combat the traditional scarcity of appropriate



Figure 6. Main causes of death by time since transplant in the 2013 to 2022 period. GVD/SCD, graft vascular disease/sudden cardiac death. Each cause of death is reported as a percentage of total patient deaths in the specific period.



Figure 7. Changes over time in the main causes of death in the first posttransplant year in the 2013 to 2022 period by 3-year period.

donors for pediatric patients. This area also encompasses donation after circulatory death. The first of this type of donation in Spain was recorded at the end of 2020 and the technique is showing an almost exponential growth. It is used for both pediatric and adult transplantation. In 2022, 9 centers in Spain already have a program with these characteristics, and the procedure is expected to represent a true revolution in the expansion of the donor supply, given that it exhibits equivalent outcomes to traditional donation after brain death.⁷

Limitations

This study has the typical limitations inherent to a registry of unaudited reports.

CONCLUSIONS

Clinical characteristics and survival outcomes have remained stable in Spain in recent years. A notable increase was detected in ABO-incompatible transplantation techniques and donation after circulatory death.

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This work has not received any funding.

AUTHORS' CONTRIBUTIONS

All authors have contributed to the data collection, have critically revised the manuscript, and have approved its publication in the current form. F. González-Vílchez drafted the manuscript.

CONFLICTS OF INTEREST

None.

APPENDIX 1. COLLABORATORS IN THE SPANISH HEART TRANSPLANT REGISTRY 1984 TO 2022

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Hospital General Universitario Gregorio Marañón (adults), Madrid	Zorba Blázquez, Iago Sousa, Javier Castrodeza, Eduardo Zataraín, Adolfo Villa y Manuel Martínez-Sellés
Hospital Univesitari i Politècnic La Fe, Valencia	Raquel López-Viella, Víctor Donoso- Trenado, Soledad Martínez-Penades, Ignacio Sánchez-Lázaro
Hospital Universitario Reina Sofía, Córdoba	Francisco Carrasco-Ávalos
Hospital Universitario Puerta de Hierro- Majadahonda, Majadahonda, Madrid	Manuel Gómez-Bueno, Javier Segovia- Cubero, Cristina Mitroi, Mercedes Rivas- Lasarte, Sara Lozano-Jiménez, Jose María Viéitez-Flórez
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