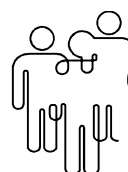


Catalan Heart Transplant Registry

1984-2007 Report



Generalitat de Catalunya
Departament de Salut



OCATT

Organització Catalana
de Trasplantaments

Catalan Heart Transplant Registry Advisory Committee

Dr. Fèlix Pérez Villa (Hospital Clínic i Provincial de Barcelona)
Dr. Josep Maria Padró (Hospital de la Santa Creu i Sant Pau)
Dr. Nicolás Manito (Hospital Universitari de Bellvitge)
Dr. Josep Girona (Hospital Universitari Maternoinfantil de la Vall d'Hebron)
Sra. Nuria Trota (Organització Catalana de Trasplantaments. Servei Català de la Salut)
Dra. Rosa Deulofeu (Organització Catalana de Trasplantaments. Servei Català de la Salut)

Notifying Centers

Hospital Clínic i Provincial de Barcelona
Hospital de la Santa Creu i Sant Pau
Hospital Universitari de Bellvitge
Hospital Maternoinfantil de la Vall d'Hebron

Person in charge of registry: R. Deulofeu, director of OCATT

Registry management: Catalan Heart Transplant Registry Advisory Committee

Registry technician: N. Trota

Data collection: N. Trota

Data analysis and written report: N. Trota

Acknowledgements

The Catalan Transplant Organization (OCATT), which is responsible for the Heart Transplant Registry of Catalonia, would like to express its appreciation to all the staff members of the centers authorized to perform heart transplants for their contribution to the maintenance of the registry by supplying data and their participation in the preparation of the report through their contributions.

Dr. Rosa Deulofeu
Director of OCATT

Address correspondence to:

Nuria Trota
Catalan Transplant Organization (OCATT)
Catalan Health Service. Ministry of Health
Mejía Lequerica, 1, pavelló Hèlios 3, 1a planta
08028 Barcelona, Spain

Email: ntrota@catsalut.cat

<http://www.gencat.ocatt.cat>

Contents

Introduction	7
Methodological aspects and definitions	8
Evolution of Heart Transplants	9
Recipient characteristics	11
Donor characteristics.....	17
Transplant characteristics.....	19
Retransplants	21
Survival	23
Mortality	27
Waiting List	30
Heart Transplants in Children	33

Introduction

In 1984, the first heart transplant carried out in Catalonia was performed at Hospital de la Santa Creu i Sant Pau. It was also the first successful heart transplant carried out in Spain. A few years later, in 1991, the Hospital Universitari de Bellvitge began working in this field, and was followed by the Hospital Clínic i Provincial de Barcelona in 1998. The Hospital Maternoinfantil de la Vall d'Hebron was authorized to perform heart and heart-lung transplants in 2002 for children and adolescents.

The Heart Transplant Registry was created in 1993 and contains data on the transplants done in Catalonia since 1984. The data on transplants carried out in the 1984-1993 period were gathered retrospectively, but, since 1994, the registry has systematically gathered data as they have become available.

Publishing the registry is one of the objectives of OCATT, as is managing the data of the Registry Advisory Committee, which responds to the information requirements on planning, resource management and the purchase of services of the Catalan Health Service and the Ministry of Health. The registry is also an information source that is accessible to external users, such as healthcare professionals, and responds to the needs of other sectors. In all cases, processing of and access to data is subject to regulations in force on the protection of personal data.

The main aim of this report is to provide information about the activity and characteristics of the heart transplants carried out in Catalonia in 2007, and to describe the evolution of the transplants carried out since 1984. This information is made available to professionals who are directly involved in this treatment, as well as members of the public administration working in the area of healthcare.

Methodological aspects and definitions

This report describes the evolution of heart transplants in Catalonia and analyses the characteristics of receivers, donors and transplants, as well as the results obtained.

The actuarial method was used to calculate the patient survival rate (time before death). The level of statistical significance of the different curves was evaluated using the Wilcoxon test (Gehan). The survival curves break off when the number of cases fell below 10.

The probability of receiving a transplant was calculated bearing in mind the competitive risk model with three events of interest: transplant, death and removal from the waiting list.

Description of indicators:

Annual transplant rate

The total number of heart transplants carried out during the year at authorized centers, regardless of the place of residence of the receiver, compared with the population of Catalonia (census of 1991, 1996 and, starting in 1997, annual census updates. National Statistics Institute). Expressed per million population (pmp).

Cumulative incidence rate by health-care region and in Catalonia

Number of patients resident in Catalonia who received a first liver transplant in a specific period of time, with respect to the population of each health-care region and the population of Catalonia. Figures per million population (pmp). The population figure for Catalonia is that of the central registry of people insured by CatSalut (10 January 2008).

Standardized cumulative incidence rate by health-care region

Standardization by age and sex of the cumulative incidence rates, using the indirect method, which allows the rates of each health-care region to be compared with the overall rate for Catalonia. The population figure for Catalonia is the adult population (15 years of age or more) of the central registry of people insured by CatSalut (10 January 2008).

Overall mortality rate

Number of patients who died in a specific period of time, compared with the total number of patients who received a heart transplant in that same time period. Expressed as a percentage.

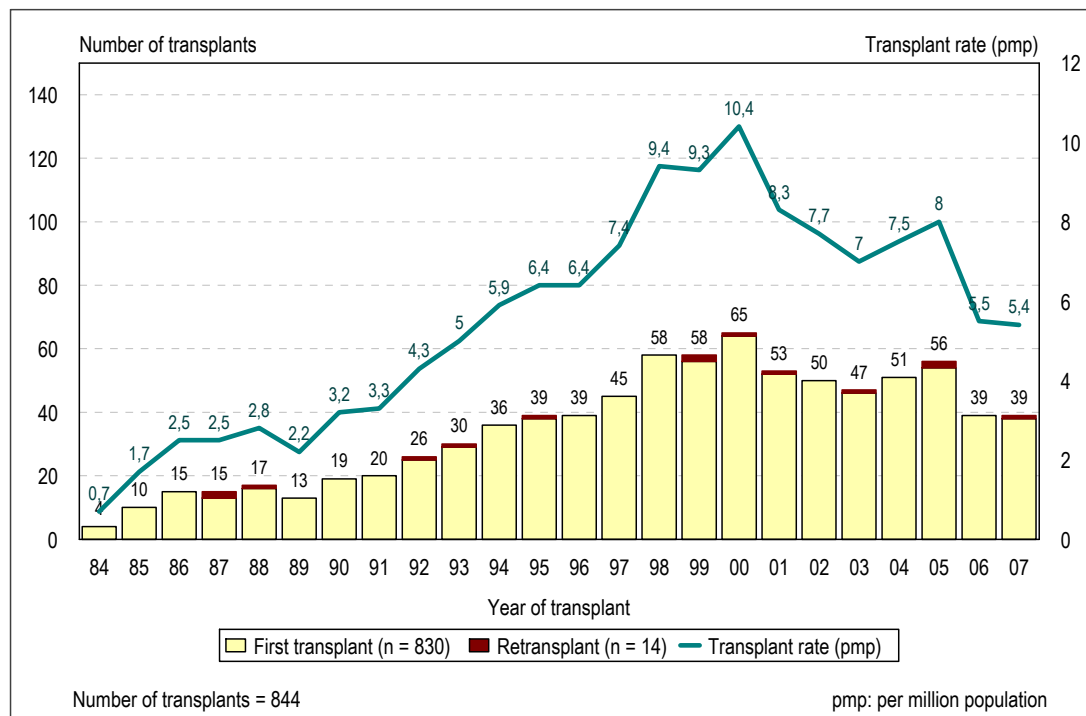
Evolution of Heart Transplants

In the 1984-2007 period in Catalonia, 844 heart transplants were performed on 830 patients (14 retransplants were performed). In 2007, 39 transplants were performed, two of which were heart-kidney transplant.

The annual evolution of the number of heart transplants has varied over the years, showing upward trends in 1992 and 1997 (years in which new centers began activity) and until 2000, when the first changes in evolution were registered (Figure 1).

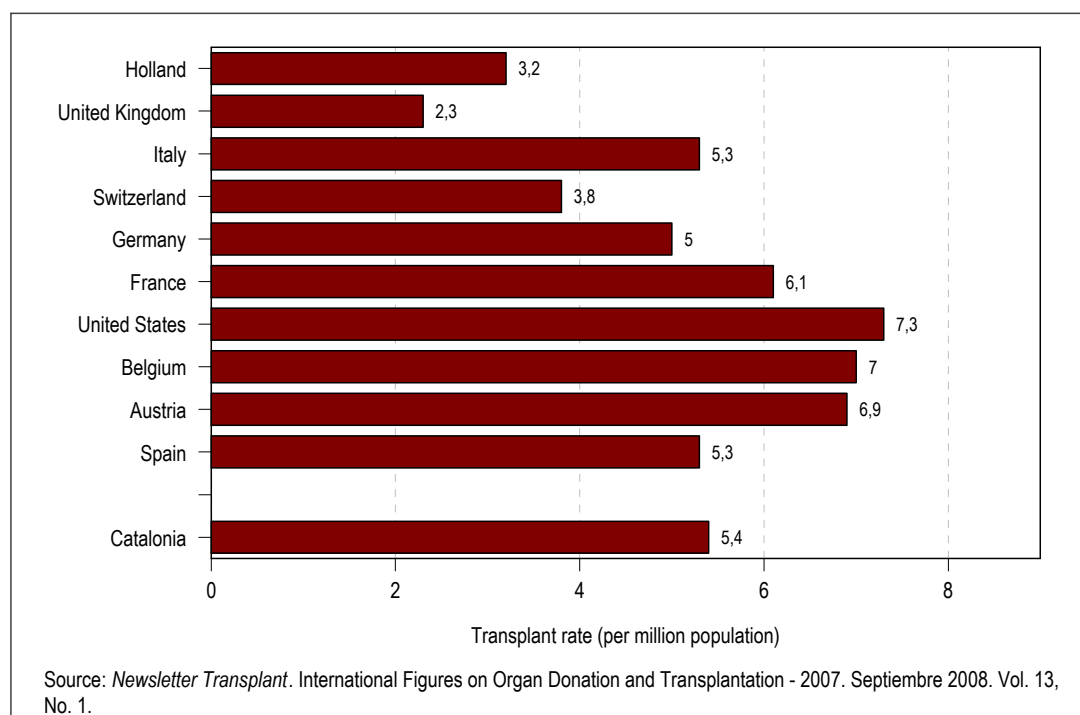
Because of these changes in trend, the annual rate of heart transplants was also affected and showed a clear upward trend in the 1992-2000 period. In 2007, the transplant rate was 5.4 per million inhabitants, which was lower than the previous year (Figure 1).

Figure 1. Annual evolution of the number of transplants and annual heart transplant rate. 1984-2007



The annual heart transplant rate varies considerably between countries. Catalonia shows one of the highest rates of transplant activity (Figure 2). However, these data should be interpreted with caution, bearing in mind different factors that affect transplant activity in each country (the healthcare system, indication criteria, population structure, etc.).

Figure 2. Heart transplant rate in different countries. 2007



Recipient characteristics

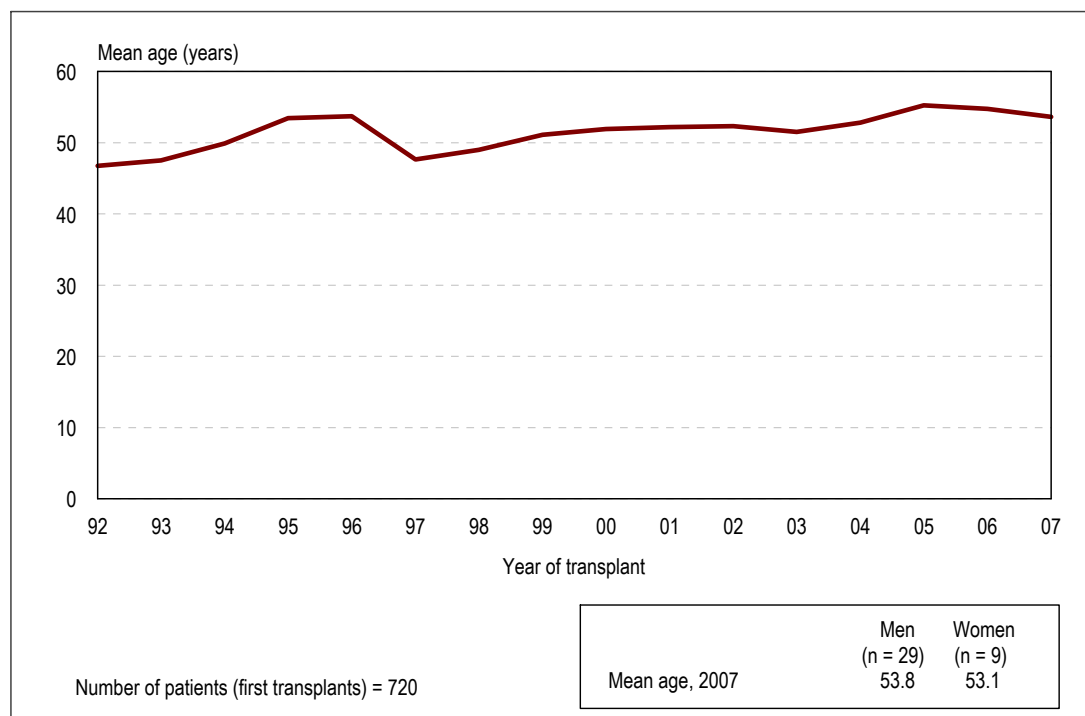
◆ Sex and age

Of the 830 patients who received transplants, 663 (79.9%) were men and 167 (20.1%) were women. These percentages remained stable in accordance with the year of the transplant.

The mean age of the patients who received their first heart transplant in the 1984-2007 period was 50 (51 for men and 48 for women), the median age was 53 and the range was from age 6 to 70.

Over the years, the mean age has increased, going from 48 in 1997 to 55 in 2007 (Figure 3).

Figure 3. Annual evolution of the mean age of patients receiving their first heart transplant. 1992-2007



In recent years, there has been a gradual increase in transplants done on patients aged 50 or more. In 2007, 47.4% of the patients who received their first transplant were between 50 and 60 and 26.3% were over 60. In 1997, these percentages were 33.3% and 20.0%, respectively (Figure 4).

63.1% of patients were over 50 when they received their first heart transplant. In fact, 51.5% of all patients were men aged 50 or more (Figure 5).

Figure 4. Annual evolution of the percentage of patients who received their first heart transplant, by age group. 1992-2007

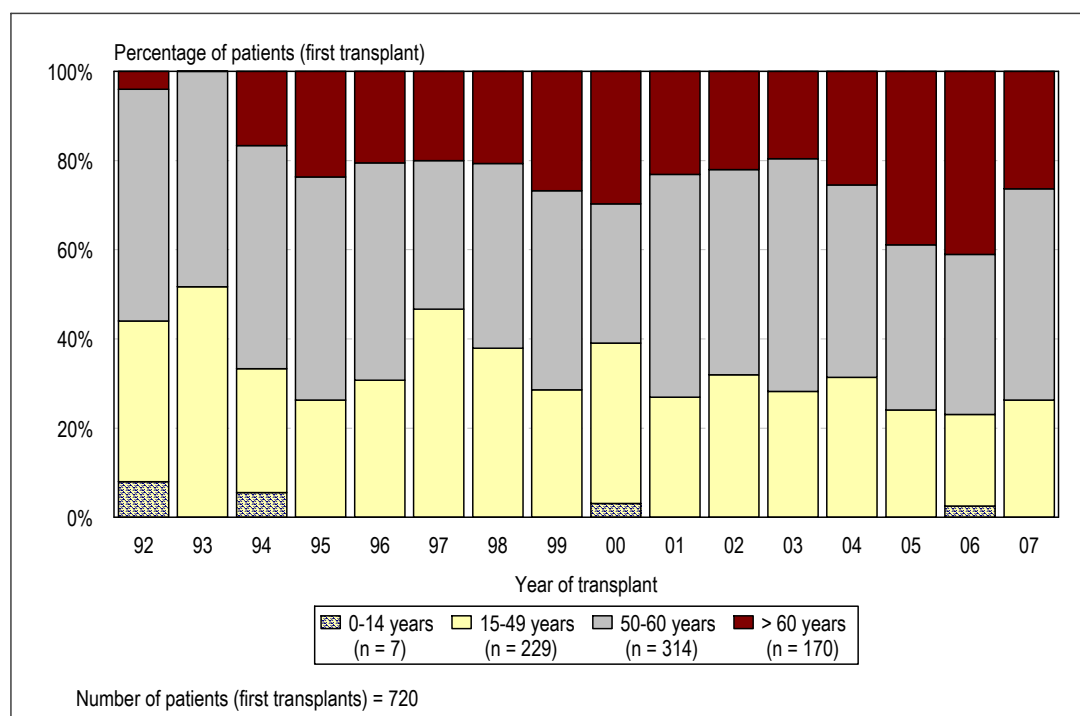
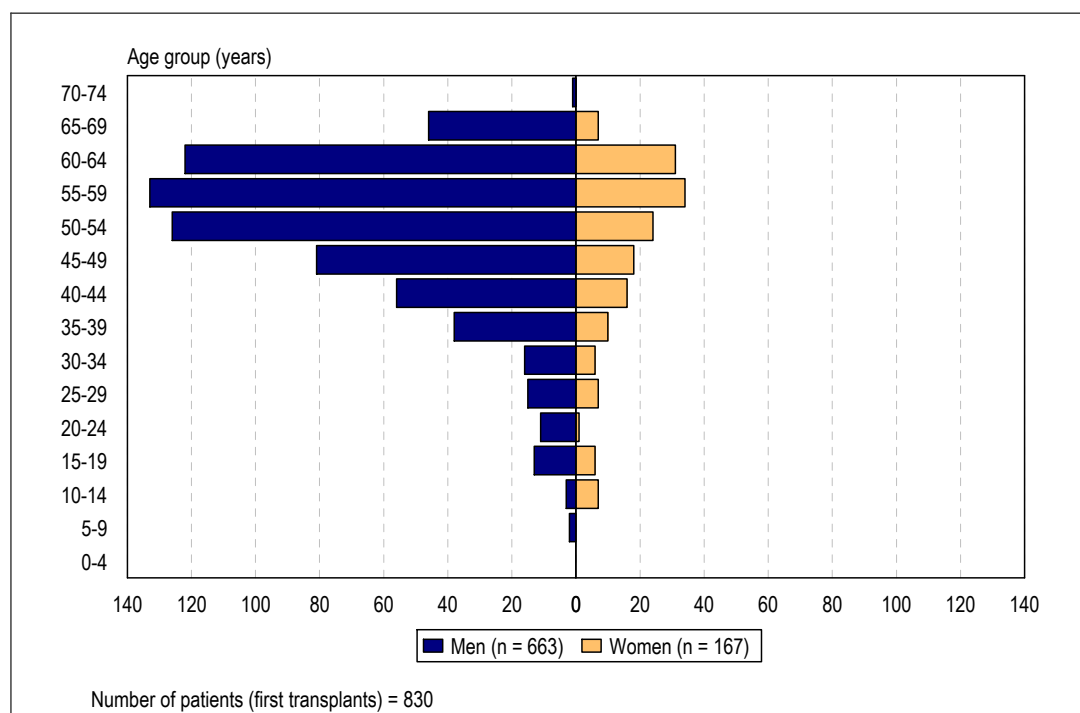


Figure 5. Number of patients who received their first heart transplant, by age group and sex. 1984-2007



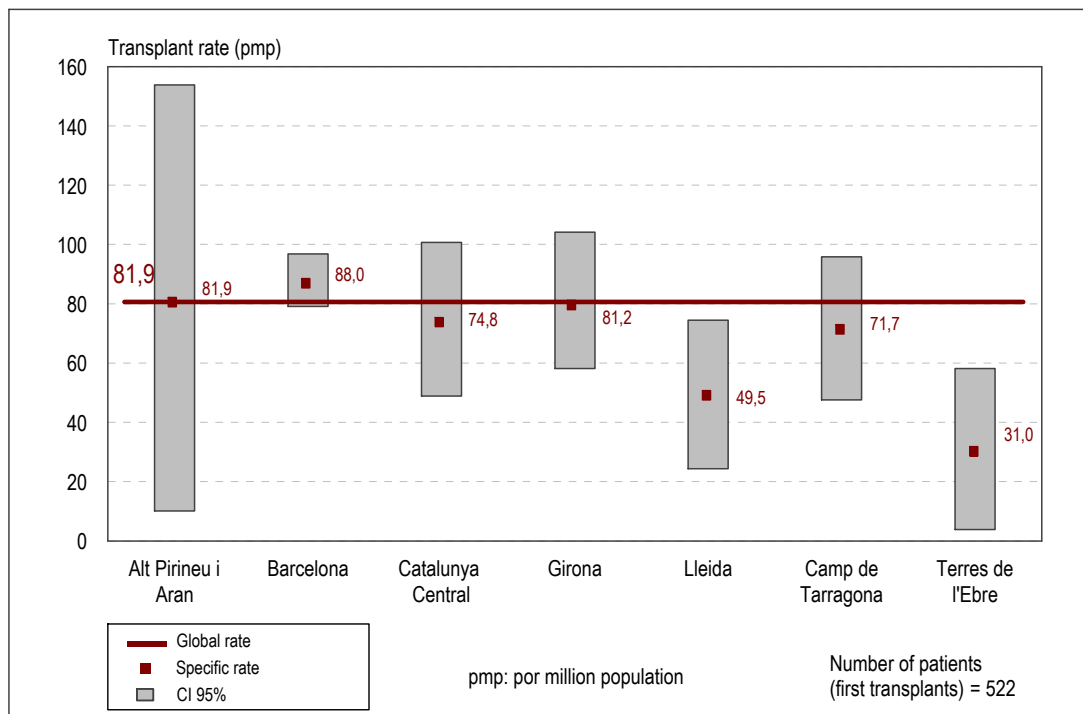
◆ Place of residence

91.9% (n = 763) of patients receiving transplants were residents of Catalonia, 8% (n = 66) were residents of another part of Spain and 0.1% (n = 1) were foreigners. In general, the patients who were not residents of Catalonia came from the Balearic Islands (n = 32) or the autonomous community of Aragon (n = 13).

Of the patients residing in Catalonia, the largest group (74.2%) belonged to the healthcare region of Barcelona, followed by residents of the healthcare regions of Girona (9.1%), Camp de Tarragona (6.6%) and Catalunya Central (5.8%). The lowest percentages were those of residents of the healthcare regions of Lleida (2.6%), Terres de l'Ebre (0.9%) and Alt Pirineu i Aran (0.8%).

Figure 6 shows the standardized cumulative incidence of patients who received their first heart transplant in the 1997-2007 period. The overall incidence for Catalonia was 81.9 per million inhabitants (pmp). Statistically significant differences were only observed in the incidences of the regions of Lleida and Terres de l'Ebre.

Figure 6. Standardized cumulative incidence of the first heart transplants in patients residing in Catalonia, by healthcare region of residence. 1997-2007



◆ Indications

The heart transplant indications are arranged in four groups: dilated cardiomyopathy, ischemic cardiomyopathy, valvular cardiomyopathy and the “other” category, which includes restrictive cardiomyopathy, congenital cardiomyopathy and hypertrophic cardiomyopathy.

Dilated cardiomyopathy (45.5%) and ischemic cardiomyopathy (39.8%) have been the two most common indications for the heart transplants carried out in Catalonia since 1984. In the case of men, 46.8% of patients suffered from ischemic cardiomyopathy and 41.8% from dilated cardiomyopathy. In the case of women, the most common indication was dilated cardiomyopathy (Figure 7).

In 2007, 36.8% (n = 14) of patients presented with dilated cardiomyopathy and 52.6% (n = 20) with ischemic cardiomyopathy. The most common indication has changed over the years. In the first few years, dilated cardiomyopathy was the most common indication, but the percentages for ischemic cardiomyopathy have now come level with those for dilated cardiomyopathy and, in some years, ischemic cardiomyopathy

has even been the most common indication. However, given the low number of transplants carried out each year, it is difficult to draw conclusions from the slight changes that arise from one year to the next (Figures 8 and 9).

Figure 7. Percentage of patients who received their first heart transplant, by indication and sex. 1984-2007

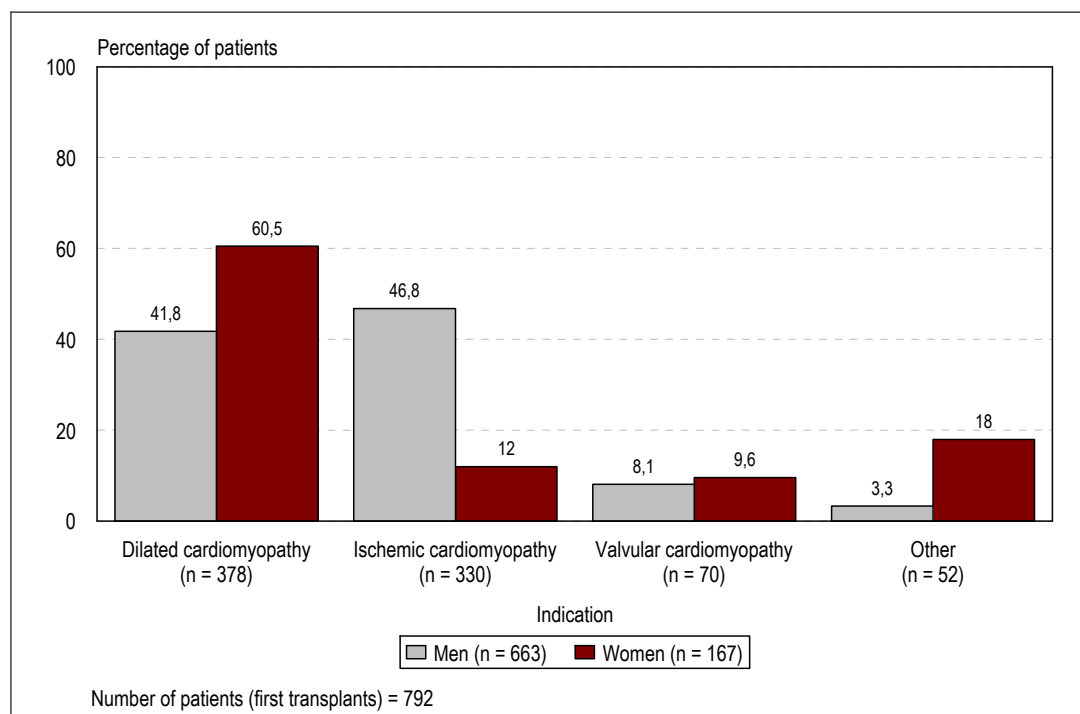


Figure 8. Annual evolution of the number of patients who received their first heart transplant, by indication. 1992-2007

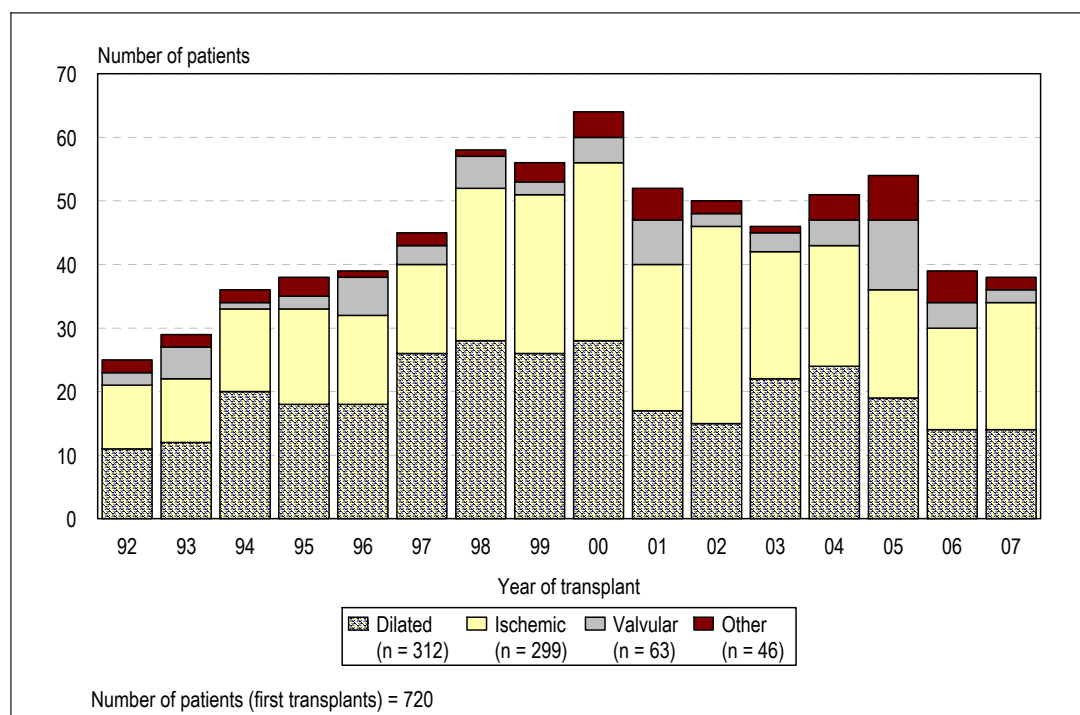
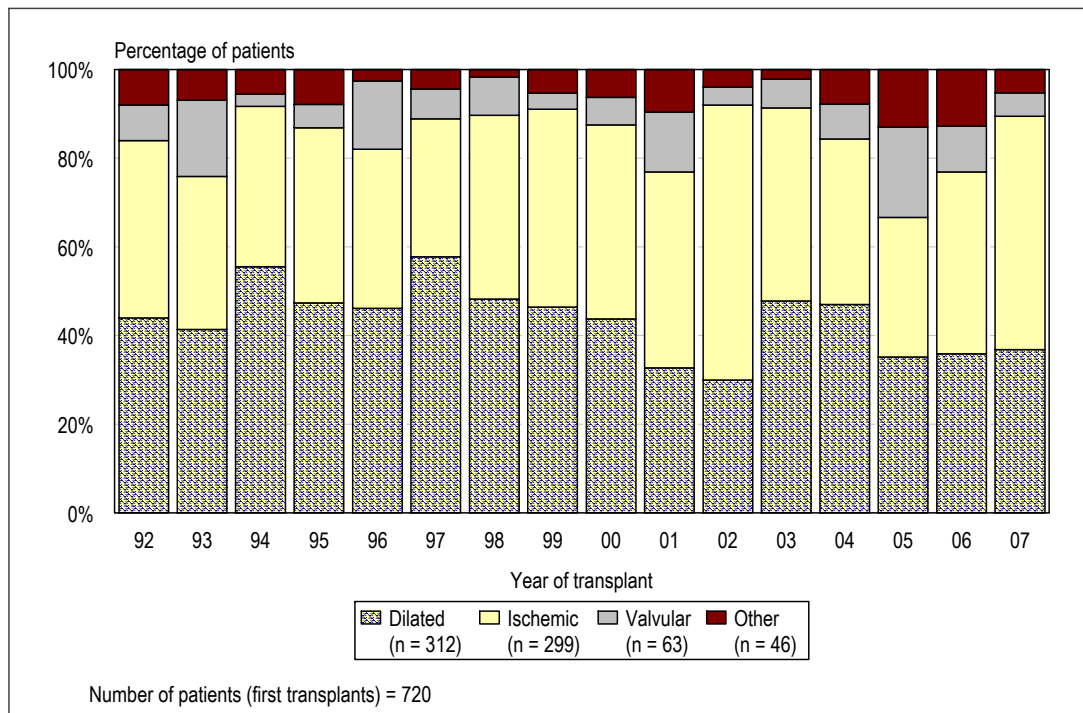
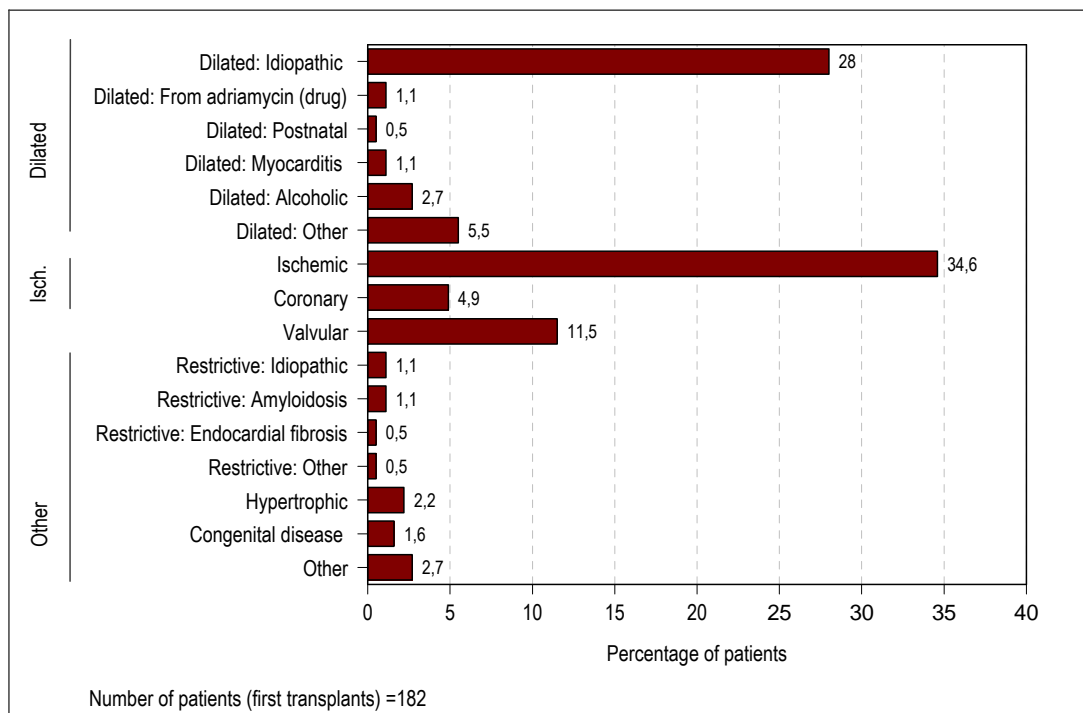


Figure 9. Annual evolution of the percentage of patients who received their first heart transplant, by indication. 1992-2007

In 2004, the registry started using a new system to classify indicated diseases so they could be accounted for more accurately. The most frequent indications in the years from 2004 to 2007 were idiopathic dilated cardiomyopathy, ischemic cardiomyopathy and valvular cardiomyopathy (Figure 10).

Figure 10. Percentage of patients who received their first heart transplant, by indication. 2004-2007

Statistically significant differences in mean age were observed between the four indications ($p < 0.0001$): the patients with ischemic cardiomyopathy or valvular cardiomyopathy were older than those who presented with dilated cardiomyopathy (Table 1). The differences between men and women when treated separately were also statistically significant (Table 2).

Table 1. Mean and confidence interval of age, by indication. 1984-2007

	n	mean	95% CI
Dilated cardiomyopathy	378	48.6	47.2 – 50.0
Ischemic cardiomyopathy	330	54.1	53.3 – 54.9
Valvular cardiomyopathy	70	53.0	50.9 – 55.1
Other forms of cardiomyopathy	52	37.3	32.6 – 42.0
Total	830	50.5	49.6 – 51.3

Table 2. Mean and confidence interval of age, by indication and sex. 1984-2007

		n	mean	95% CI
Dilated cardiomyopathy	Men	277	48	46.3 – 49.7
	Women	101	50,4	47.9 – 53.0
Ischemic cardiomyopathy	Men	310	54,2	53.3 – 55.0
	Women	20	53,2	49.4 – 57.1
Valvular cardiomyopathy	Men	54	53,3	51.0 – 55.6
	Women	16	52,0	46.4 – 57.6
Other forms of cardiomyopathy	Men	22	39,3	31.4 – 47.2
	Women	30	35,8	29.7 – 41.9
Total	Men	663	51,0	50.1 – 51.9
	Women	167	48,3	46.1 – 50.4

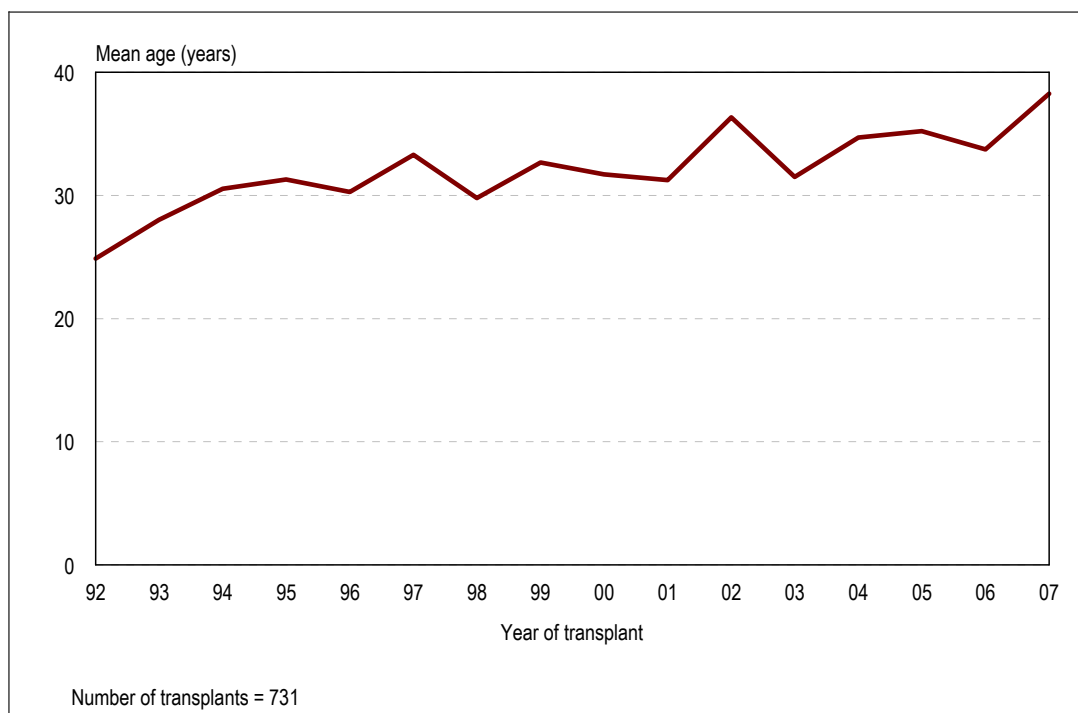
Donor characteristics

♦ Sex and age

Of the 805 transplants carried out in the 1984-2007 period, 70.8% of the donors were men and 29.2% were women.

The mean age of the donor over the entire period was 31, the median age was 30 and the range was from age 5 to 64. The mean age has increased over the years, going from 25 in 1992 to 38 in 2007 (Figure 11).

Figure 11. Evolution of the mean age of the donor. 1992-2007



♦ Cause of death

The most frequent cause of death of the donor was head trauma (HT), which represented 56.3% of all causes, followed by cerebrovascular accident (CVA) / stroke, which represented 34.7%. In 2007, 41.0% of the donors died from HT and 43.6% from CVA (Figure 12).

♦ Origin

23.3% (197) of the transplanted organs came from the same hospital where the transplant was carried out, 45.1% (381) from other hospitals in Catalonia, and 31.5% (266) from hospitals outside Catalonia. In 2007, 17.9% of the organs came from the same hospital, 48.7% from Catalonia, and 33.3% from outside Catalonia (Figure 13).

Figure 12. Evolution of the cause of death of donor (%). 1992-2007

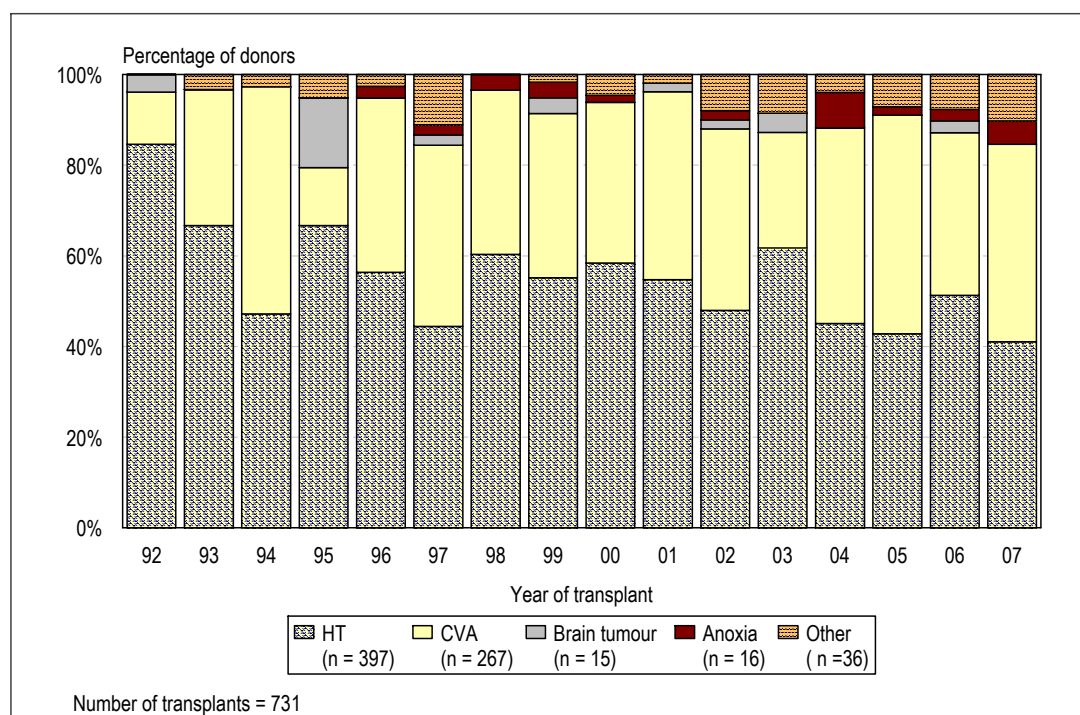
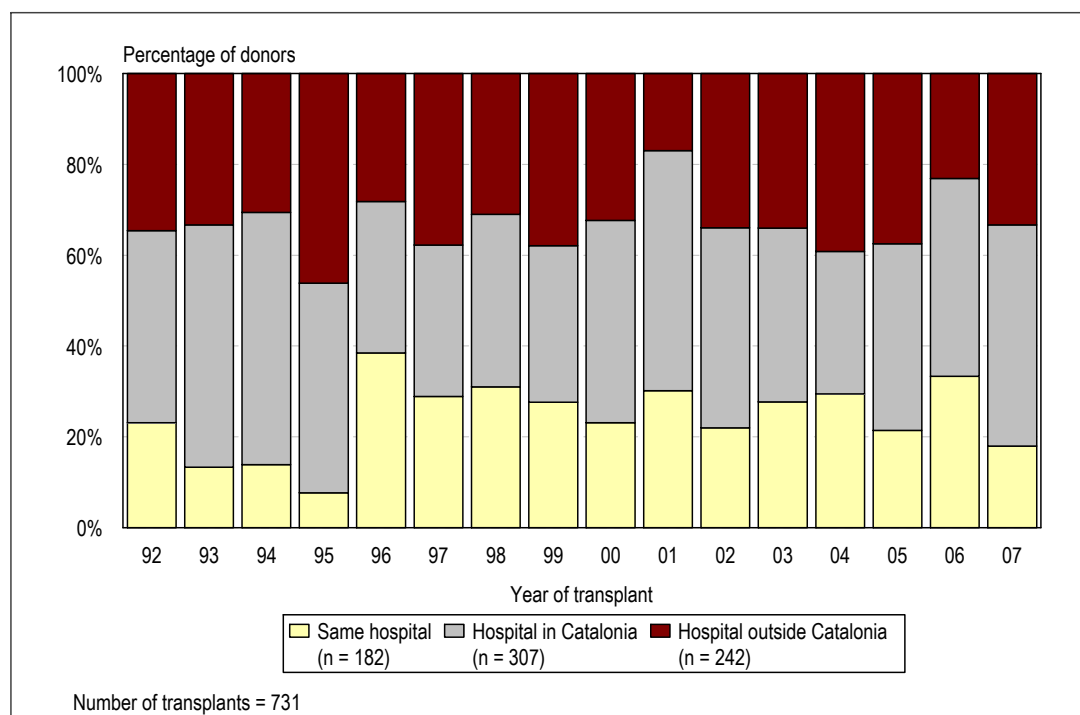


Figure 13. Evolution of donor origin (%). 1992-2007



Transplant characteristics

♦ Urgency

Of the 400 transplants carried out in the 2000-2007 period, 18.0% (72) were urgent. Nine (23.1%) of the 39 transplants carried out in 2007 were urgent (Figure 14).

Figure 14. Annual evolution of the percentage of urgent transplants. 2000-2007



♦ Ischemia time

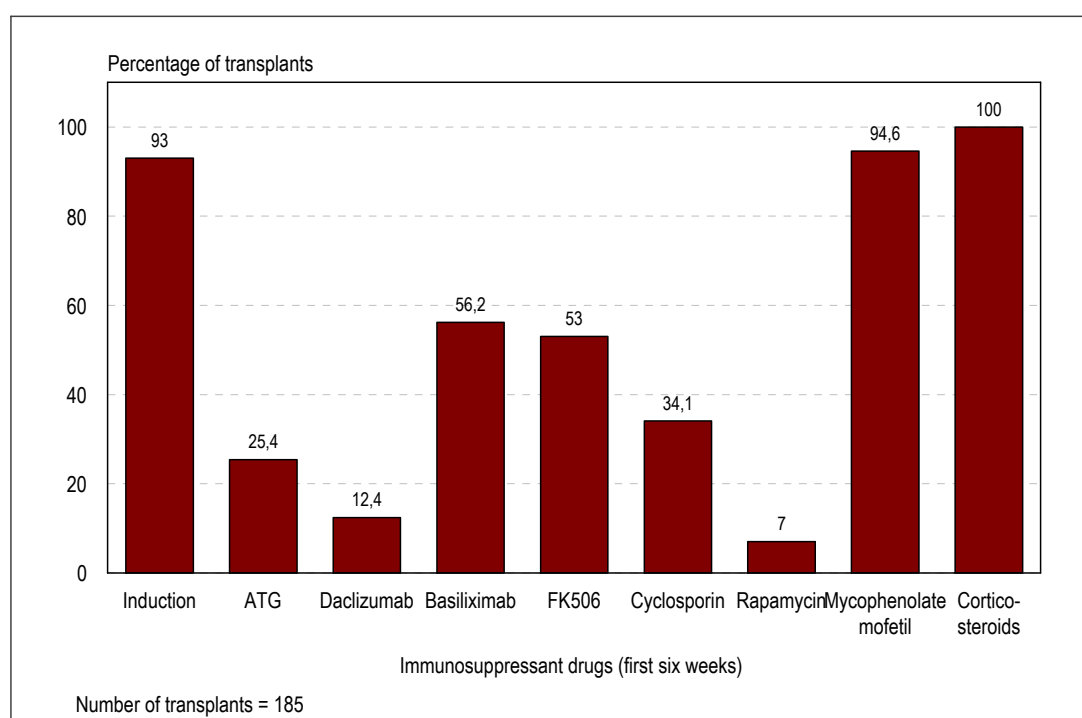
The mean ischemia time was 169 minutes. Bearing in mind the source of the organ, the differences observed were statistically significant ($p < 0.0001$). When the organ came from a hospital outside Catalonia, the mean cold ischemia time was 75 minutes higher than when the organ came from a hospital in Catalonia (Table 3).

♦ Immunosuppressors

The distribution of immunosuppressors used in the first six weeks after transplant is shown in Figure 15. The majority of transplanted patients take induction immunosuppression, being Basiliximab the most common.

Table 3. Cold ischemia time, in minutes, in accordance with the source of the organ. 1984-2007

	Same Hospital (n = 194)	Hospital in Catalonia (n = 375)	Hospital outside Catalonia (n = 260)	Total (n = 829)
Mean	130	151	224	169
Median	125	147	226	160
Range	60 – 230	64 – 295	105 – 360	60 – 360
95% CI	126 – 135	146 – 155	220 – 229	165 – 173

Figure 15. Immunosuppressant drugs used in the first six weeks after heart transplant. 2004-2007

Retransplants

Of the 844 transplants carried in the 1984-2007 period, 14 were retransplants.

The time between one transplant and the other ranged from 0 to 13 years. The mean was 4.5 years (the median was 4 years). Specifically, 3 (21.4%) patients received a second transplant in the first week after receiving the first, 3 (21.4%) between the first week and three months after receiving the first transplant, and 8 (57.1%) after the first year.

Tables 4 and 5 show the main characteristics of the retransplants.

Table 4. Characteristics of the patients who received a retransplant, by the time elapsed since the first transplant. 1984-2007

	0-3 months	> 3 months
Sex		
Male	5 (83.3%)	6 (75.0%)
Female	1 (16.7%)	2 (25.0%)
Age (years)		
Mean	44.8	33.1
Median	42.5	38.5
Range	35 – 63	15 – 43
Indication		
Dilated cardiomyopathy	2 (33.3%)	6 (75.0%)
Ischemic cardiomyopathy	3 (50.0%)	2 (25.0%)
Valvular cardiomyopathy	-	-
Other cardiomyopathy	1 (16.7%)	-

Of the patients who received a retransplant in the first three months after the first transplant, three had died (two by infection) at 31 December 2007. Of the patients who received a retransplant after the third month, five had died at 31 December 2007: one due to graft vascular disease, two due to primary dysfunction of the graft and two due to other causes.

Table 5. Characteristics of the donor and the transplant (first transplant), by the time elapsed since the first transplant. 1984-2007

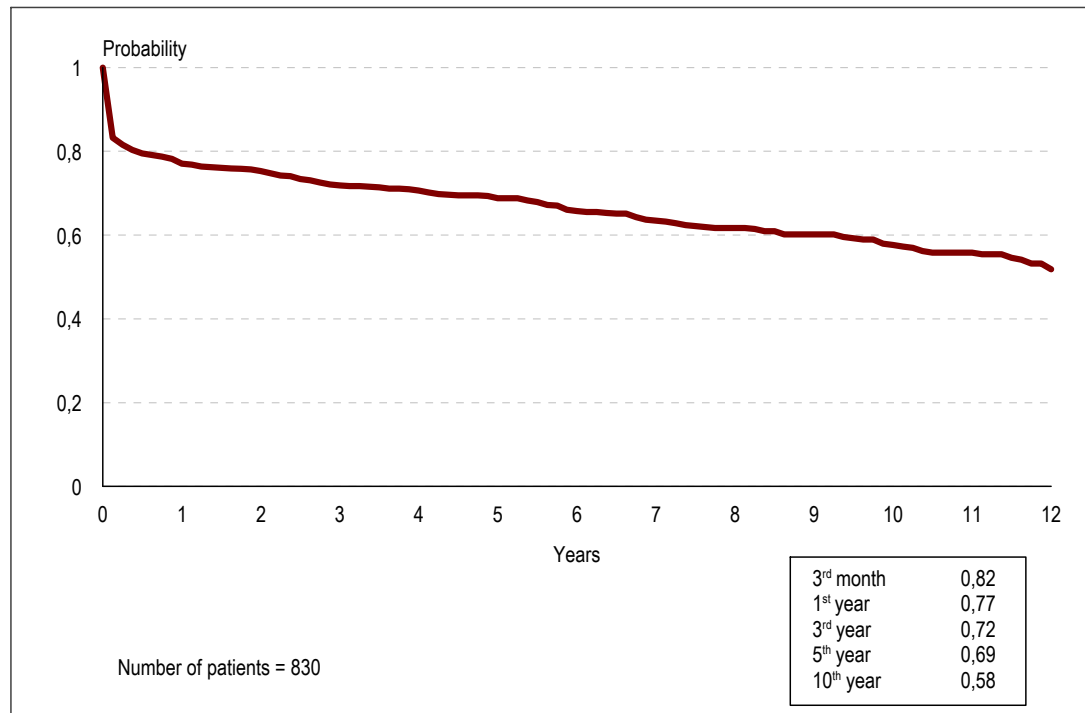
	0-3 months ¹	> 3 months
Donor age (years)		
Mean	22.0	26.3
Median	23.0	22.5
Range	17 – 25	14 – 49
Cause of donor's death		
HT	5 (83.3%)	6 (75.0%)
CVA	-	2 (25.0%)
Other	1 (16.7%)	-
Ischemia time (minutes)		
Mean	135.4	148.0
Median	115.0	131.5
Range	82 – 230	95 – 300

¹ In one case, the ischemia time was not available.

Survival

The survival rate of patients receiving a heart transplant in Catalonia in the 1984-2007 period was 82% in the first three months, 77% in the first year, 72% in the third year, and 69% in the fifth year (Figure 16).

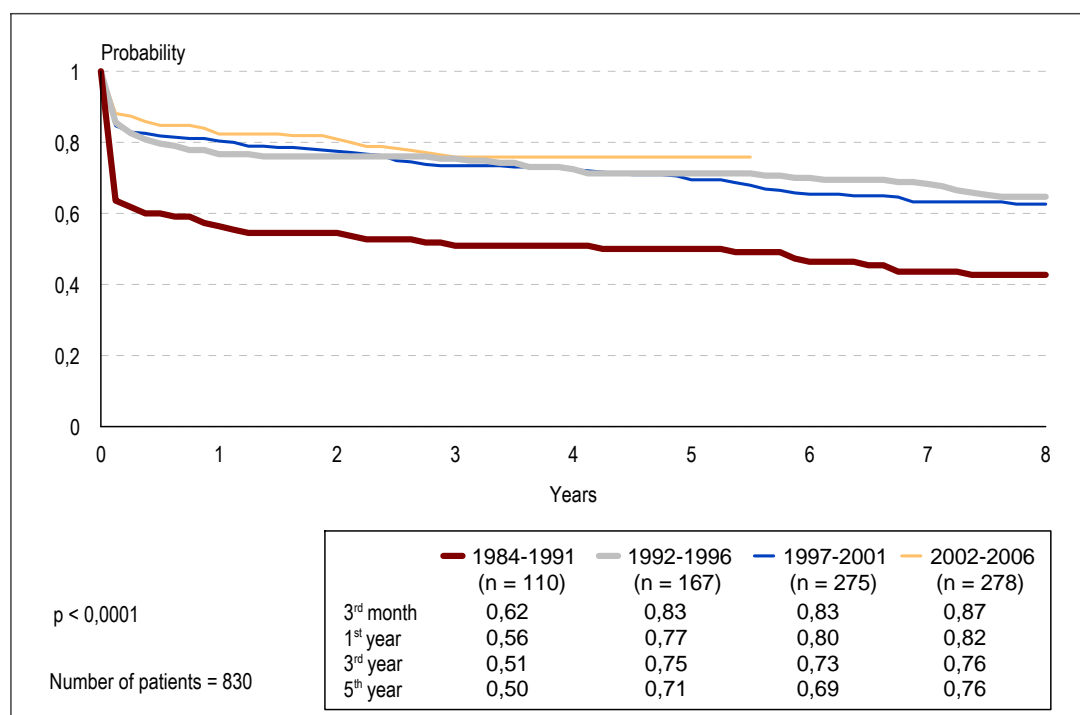
Figure 16. Survival rate of patients receiving a heart transplant. 1984-2007



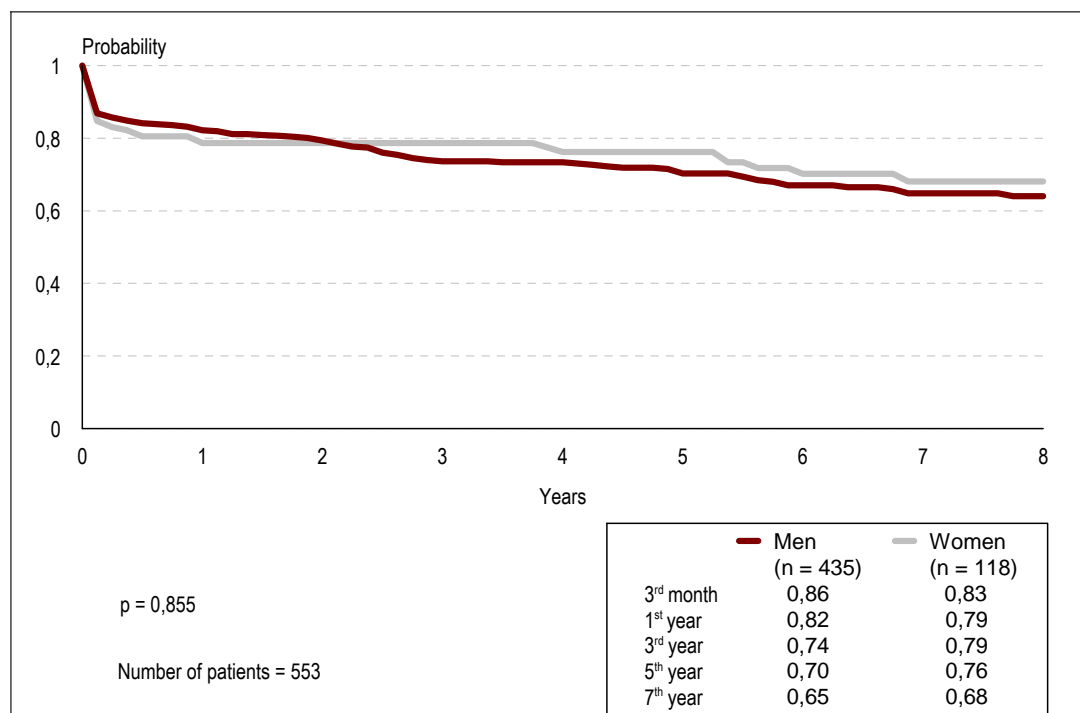
The overall patient survival rate in the 1984-2007 period was affected by the characteristics of the transplants carried out in the first few years (low number of cases, learning period) and by the factors of subsequent years (the inclusion of older patients and patients with a more negative prognosis).

The study by period was divided into four time intervals: 1984-1991, 1992-1996, 1997-2001 and 2002-2007. Statistically significant differences were observed between the four periods ($p < 0.0001$), but not between the last three (Figure 17).

In order to gain a more up-to-date look at the results, survival rates were prepared with data on the transplants carried out since 1997. In the 1997-2007 period, the patient survival rate was 85% in the third month, 81% in the first year, 75% in the third year, 72% in the fifth year, and 66% in the seventh year.

Figure 17. Survival rate of patients receiving a heart transplant, by period. 1984-2007

The survival rate of men was slightly higher than that of women (Figure 18), though these differences were not statistically significant ($p = 0.855$).

Figure 18. Survival rate of patients receiving a heart transplant, by sex. 1997-2007

The differences in the survival rates of different age groups (except for patients under age 15 when they received their first transplant) were not statistically significant (Figure 19).

Figure 19. Survival rate of patients 15 and older receiving their first heart transplant, by age group. 1997-2007

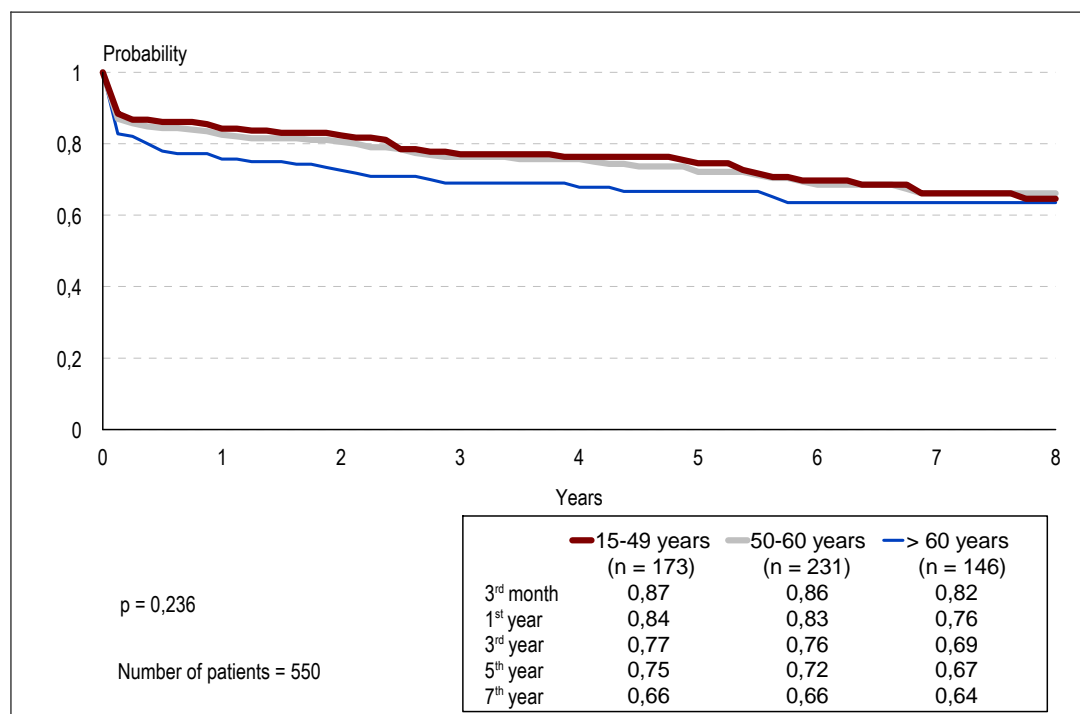
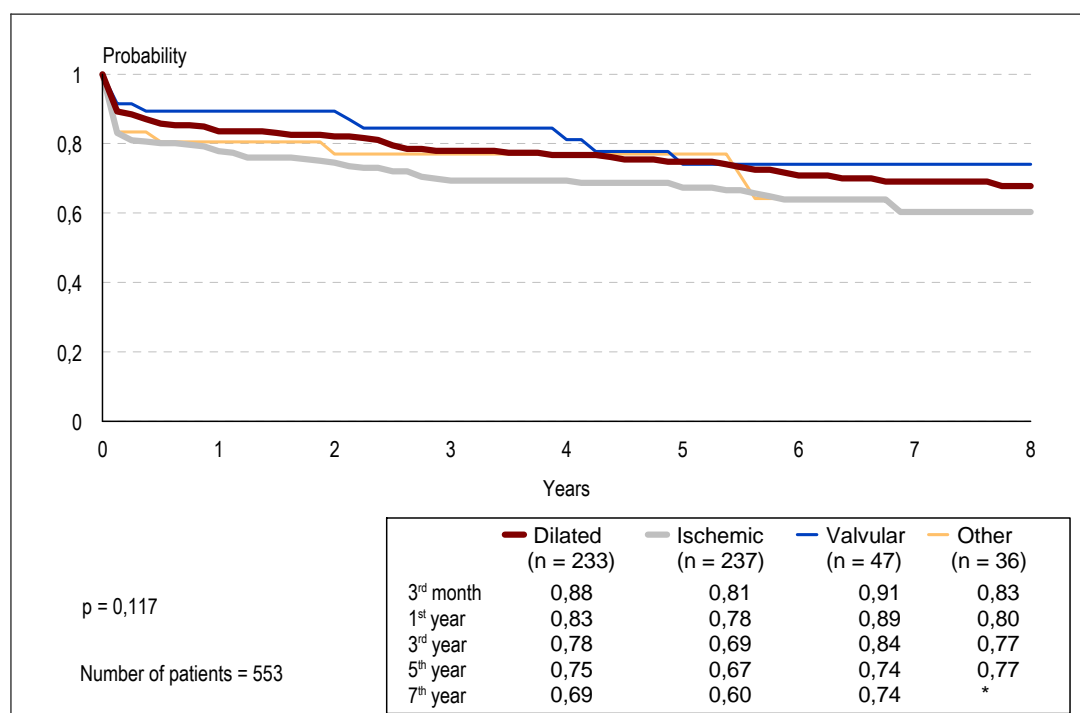


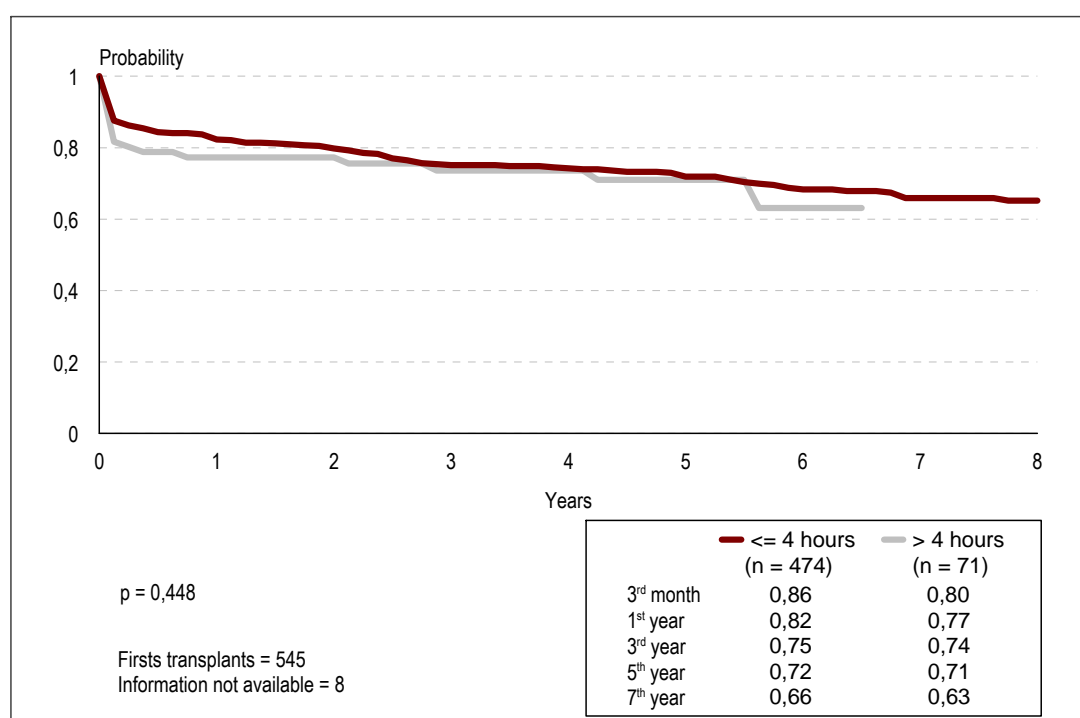
Figure 20. Survival rate of patients receiving a heart transplant, by indication. 1997-2007



Bearing in mind the indication, the patients with valvular cardiomyopathy showed a higher survival rate than patients with ischemic cardiomyopathy, which had the lowest survival rate (Figure 20). The differences between the four diagnostic groups were not statistically significant ($p = 0.117$), but the differences were statistically significant between the two most represented indications ($p = 0.045$).

When the survival rate was analysed based on the time elapsed between the extraction of the organ and the time of the transplant, it was observed that the probability of survival was greater when the cold ischemia time was less than or equal to four hours, though the differences were not statistically significant ($p = 0.448$) (Figure 21). The greatest differences were seen over the short term.

Figure 21. Survival rate of patients receiving a heart transplant, by ischemia time. 1997-2007

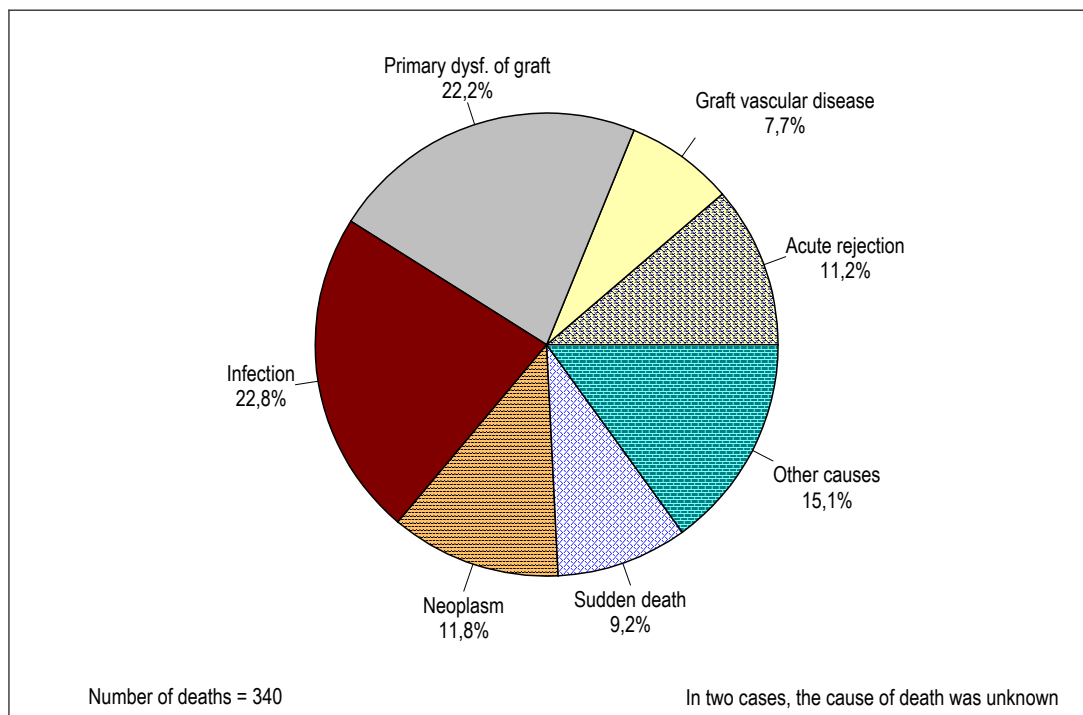


Mortality

Of the 830 patients receiving a transplant in the 1984-2007 period, 340 (41.0%) had died at 31 December 2007, 488 (58.8%) remained alive, and monitoring could not be continued on 2 (0.2%).

The most common causes of death were infection (22.8%) and primary dysfunction of the graft (22.2%), followed by neoplasm (11.8%) and acute rejection (11.2%). The first two causes alone accounted for more than 40% of all deaths (Figure 22).

Figure 22. Percentage of deaths, by cause of death. 1984-2007



When the sex of the patient was considered, these four causes of death were the same, except that the order of importance changed (Figure 23).

When the causes of death were studied by period, it was observed that the percentage of deaths due to primary dysfunction of the graft, graft vascular disease and acute rejection showed a downward trend over time. These three causes represented 56% in 1984-1991 period, in the following periods they represent 30% and 37% (Figure 24).

Figure 23. Percentage of deaths, by cause of death and sex. 1984-2007

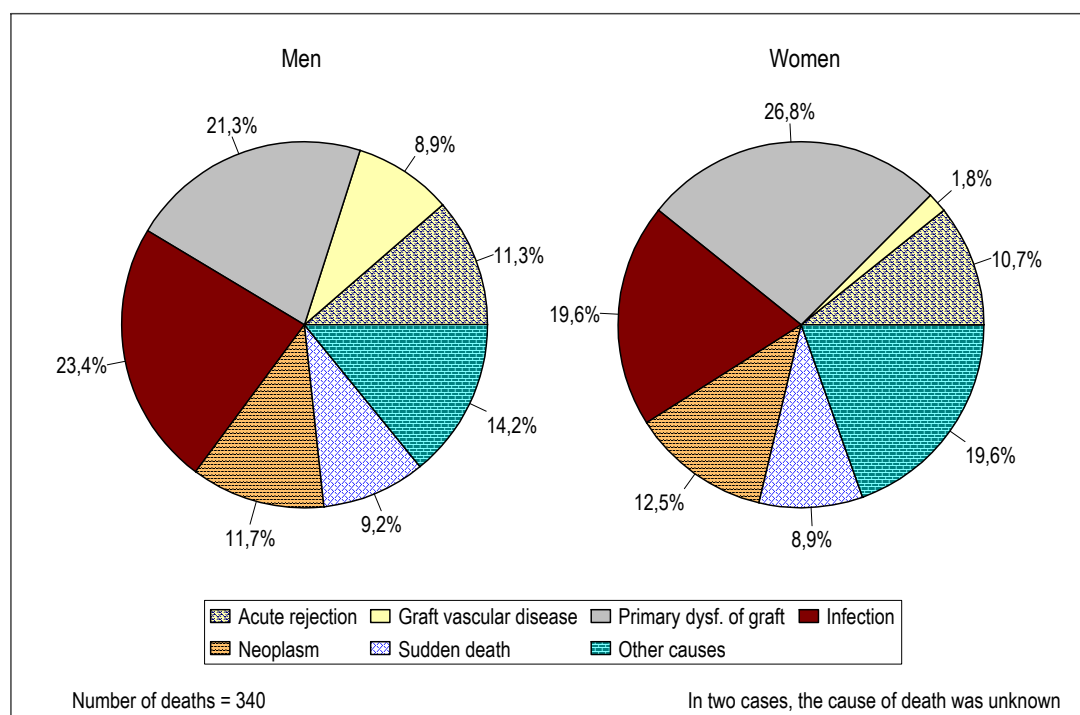
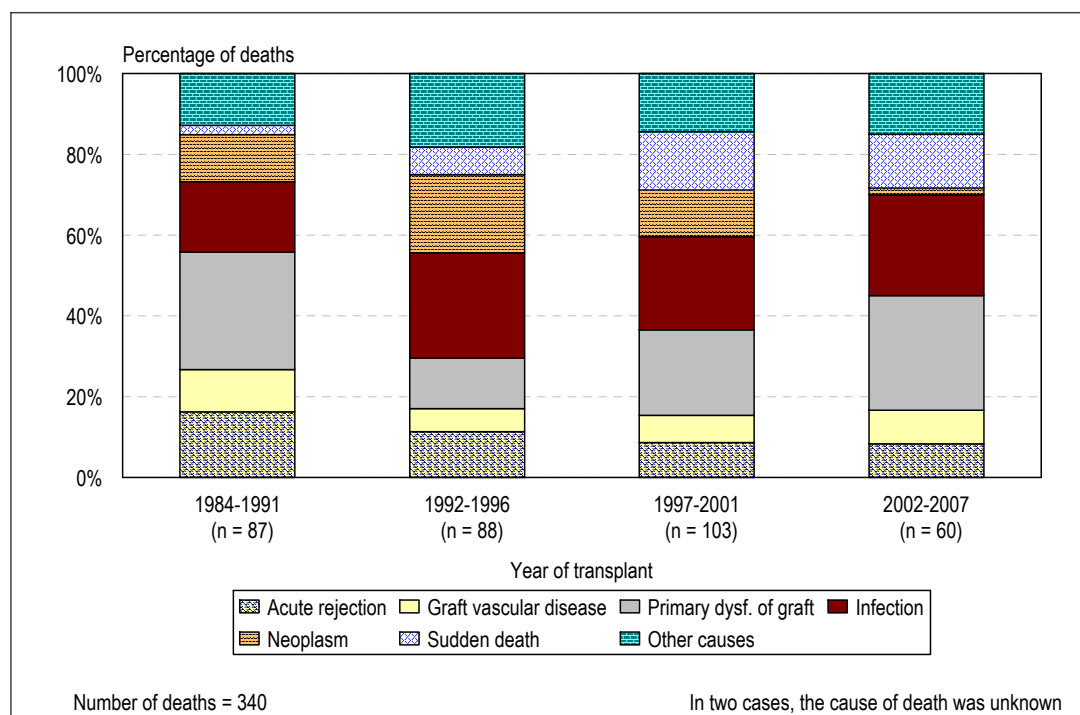
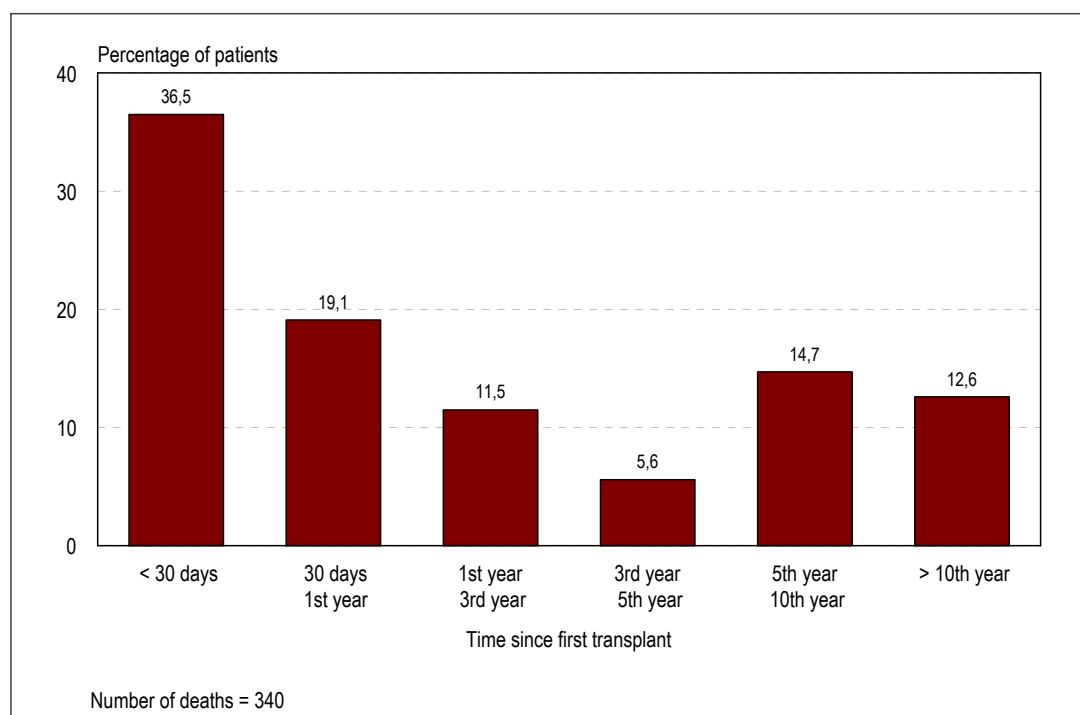
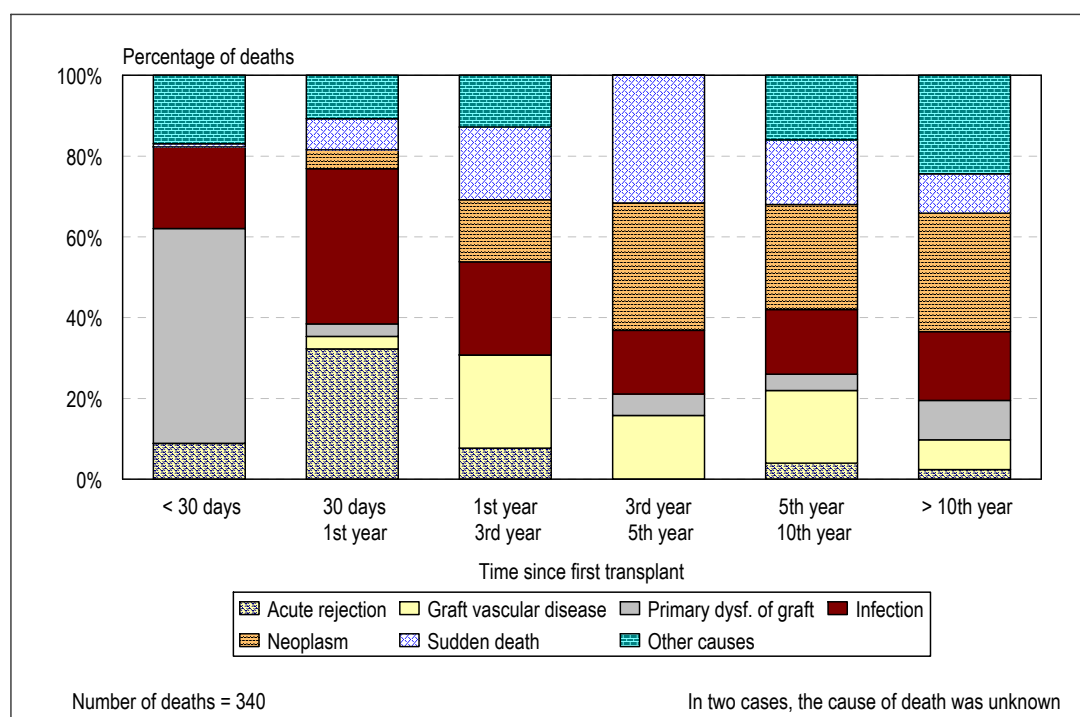


Figure 24. Percentage of deaths, by cause of death and period. 1984-2007



Death occurred in the first month after the first transplant in 36.5% (124) of cases (Figure 25), the most common cause of death being the primary dysfunction of the graft (Figure 26).

Figure 25. Deceased patients by time elapsed between transplant and death. 1984-2007**Figure 26.** Percentage of deaths, by cause of death and time elapsed between transplant and death. 1984-2007

Waiting List

The number of patients on the waiting list at the end of 2007 was upper than in previous years, going from 16 to 26, though the overall evolution of the waiting list showed an upward trend (Figure 27).

Figure 27. Evolution of the waiting list and the number of heart transplants. 1990-2007

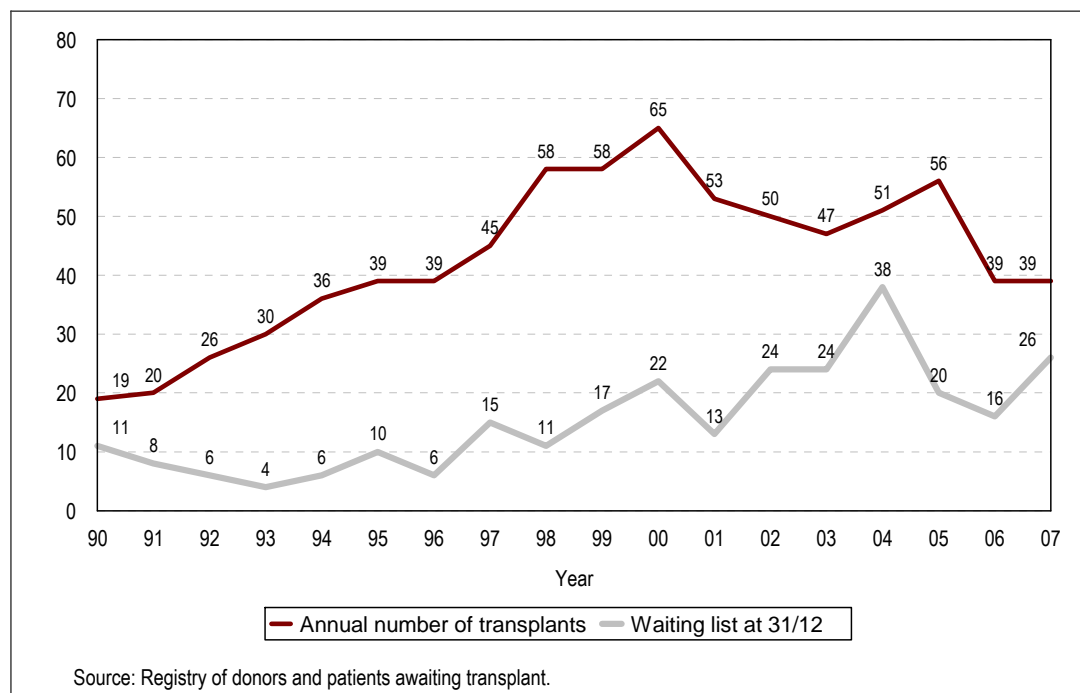
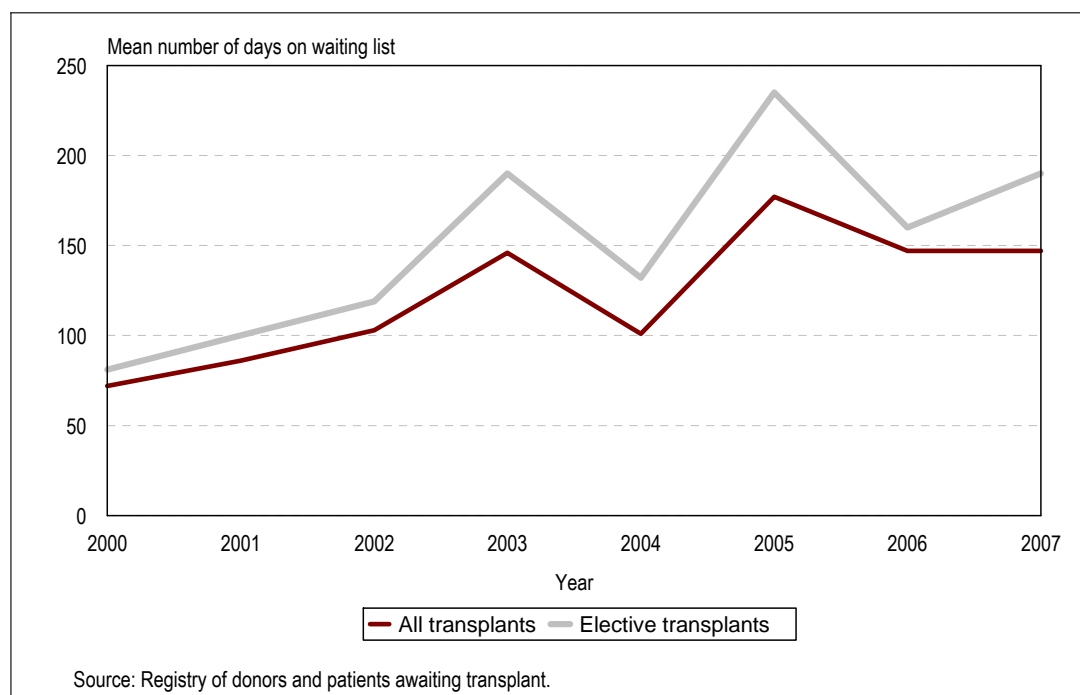


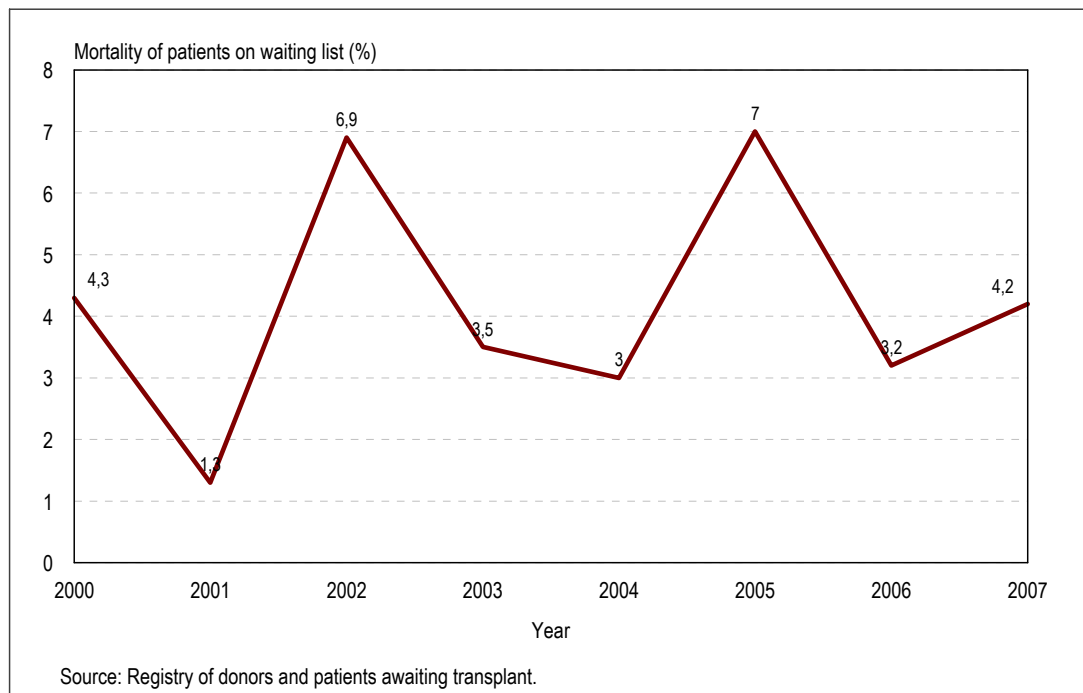
Figure 28. Mean number of days on the waiting list to receive a heart transplant. 2000-2007



In 2007, the mean number of days a patient was on the waiting list for a heart transplant was 147; if urgent transplants are excluded, the mean number of days went up to 190 (Figure 28).

In 2007, 67 patients were added to the waiting list. Of the patients taken off the list, three were removed because their health improved and five were removed because their health worsened. The mortality rate of the patients on the waiting list was 4.2%, which was upper than the previous year. Because of the low number of cases in recent years, the major fluctuations observed should be evaluated with caution (Figure 29).

Figure 29. Mortality of patients on the waiting list to receive a heart transplant (%). 2000-2007



In the 2000-2007 period, the probability of receiving a heart transplant in the first six months on the waiting list was 57%; in the first year, it was 71% (Figure 30).

When the probability of receiving a transplant was analyzed bearing in mind the patient's blood type, it was observed that for patients with blood type A, the probability (54% in the first six months and 70% in the first year) was slightly higher than patients with blood type O (55% in the first six months and 67% in the first year). Patients with blood type B and AB had higher probabilities, but these probabilities were unstable due to the low number of cases (Figure 31).

Figure 30. Probability of receiving a heart transplant. 2000-2007

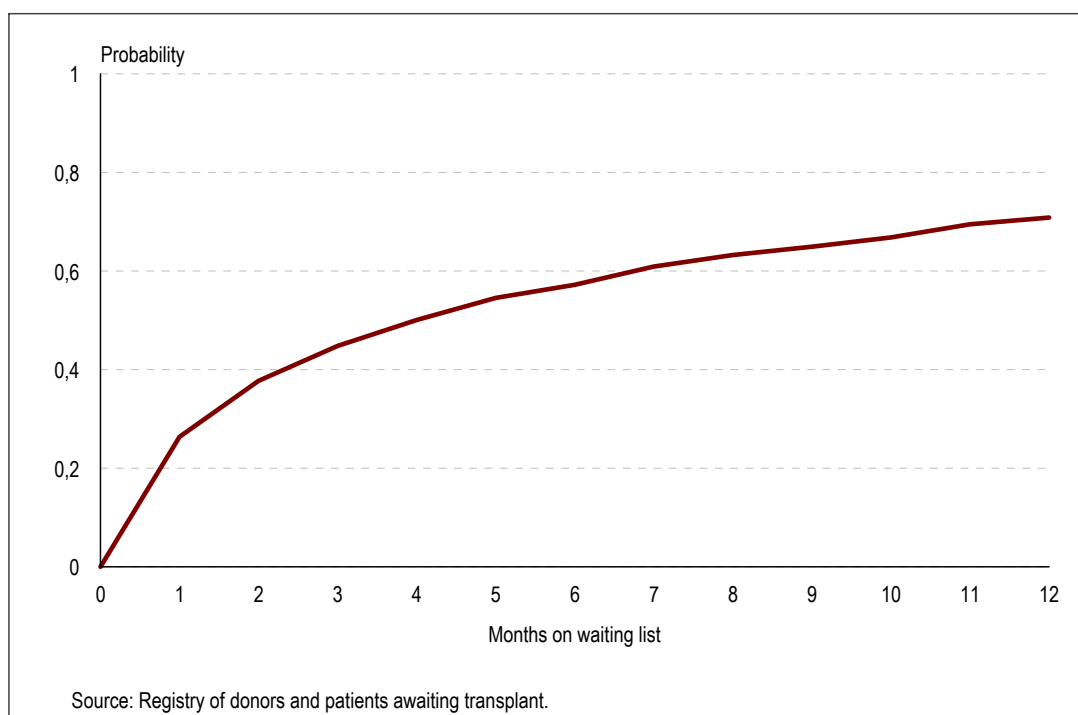
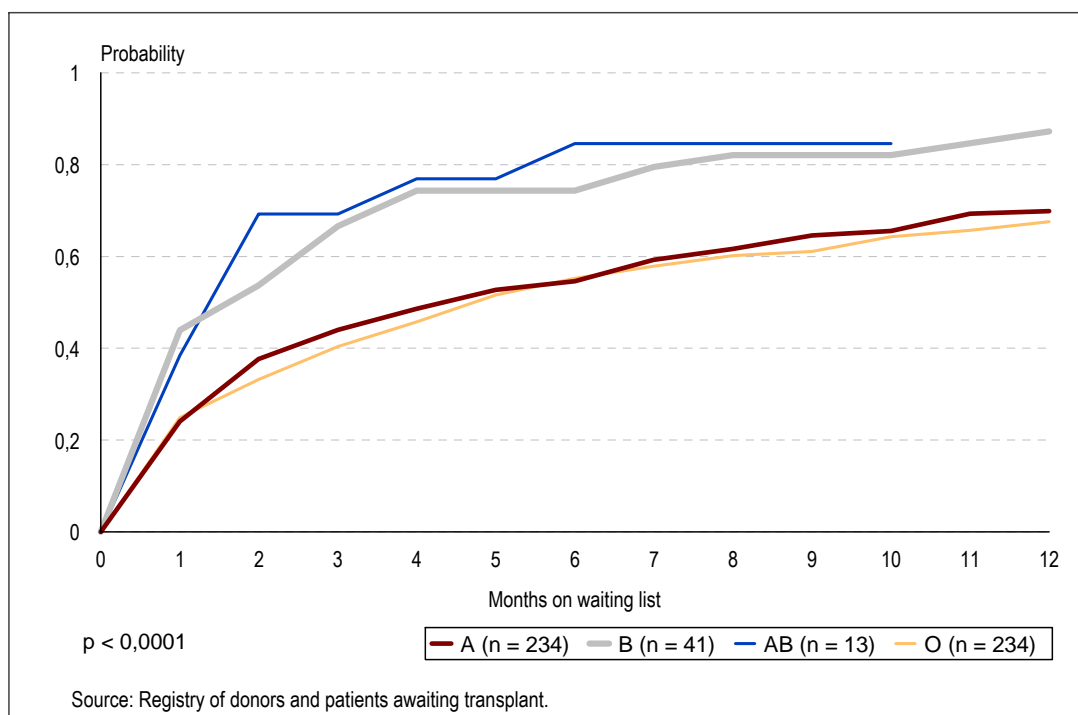


Figure 31. Probability of receiving a heart transplant, by blood type. 2000-2007



Heart Transplants in Children

Of the 792 patients receiving a transplant, 12 received their first transplant as children (up to age 14).

Six of the patients presented with dilated cardiomyopathy and the other six with other kinds of cardiomyopathy that were neither ischemic nor valvular. Specifically, three suffered from congenital cardiomyopathy, one from hypertrophic cardiomyopathy, one from arrhythmogenic right ventricular dysplasia, and the last from restrictive cardiomyopathy (Table 6).

Table 6. Characteristics of patients receiving their first transplant as children (up to age 14). 1984-2007

Sex	
Male	5 (41.7%)
Female	7 (58.3%)
Age	
Mean (\pm SD)	12 (\pm 2.6)
Median	13
Range	6 – 14
Indications	
Dilated cardiomyopathy	6 (50.0%)
Ischemic cardiomyopathy	-
Valvular cardiomyopathy	-
Other forms of cardiomyopathy	6 (50.0%)

At 31 December 2007, five of these patients had died. Two of them died in the first month after the transplant.

None of these patients received a second transplant, either as children or adults.

Table 7 shows the characteristics of the donor and the transplants carried out on children.

Table 7. Characteristics of donors and transplants in patients receiving transplants as children (up to age 14). 1984-2007

Sex of donor	
Male	2 (16.7%)
Female	3 (25.0%)
Information unavailable	7 (58.3%)
Age of donor	
Mean (\pm SD)	19 (\pm 7.5)
Median	18
Range	5 – 30
Cause of death of donor	
HT	10 (83.3%)
CVA	1 (8.3%)
Other	1 (8.3%)
Source of organ	
Same hospital	4 (33.3%)
Hospital in Catalonia	3 (25.0%)
Hospital outside Catalonia	5 (41.7%)
Ischemia time (minutes)	
Mean (\pm SD)	151 (\pm 48.6)
Median	160
Range	60 – 216