

# Catalan Heart Transplant Registry

Report 2002 -2003



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## Introduction

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The first heart transplant unit in Catalonia started operating in 1984 at the Hospital de la Santa Creu i Sant Pau. Some years later, in 1991, the Hospital de Bellvitge Prínceps d'Espanya began its activity in this field and was followed in 1998 by the Hospital Clínic i Provincial de Barcelona. Later, in the year 2002, the Vall d'Hebron Mother and Children's Hospital was given authorisation to carry out heart and lung transplants on child patients.

The heart transplant registry was set up in 1993 and it contains data on those transplants carried out in Catalonia since the year 1984. The data on the transplants carried out during the 1984-1993 period were compiled retrospectively, but since the year 1994, data for the registry are obtained periodically and systematically.

In line with its objectives, the registry responds to the information requirements of the Catalan Health Service and the Spanish Department of Health and Social Security for planning, resources management and the purchasing of services. The registry is also an accessible source of information for external users, such as healthcare professionals, and responds to the requirements of other sectors. In all cases, processing of and access to data is subject to the legal regulations in force regarding the protection of data of a personal nature.

The main objective of this document is to offer an overview of the activity and characteristics of heart transplants performed in Catalonia in the years 2002 and 2003, as well as the evolution of all those carried out since 1984, both for professionals directly involved in this treatment and those working with the Health Administration.

## Evolution of Heart Transplants

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In Catalonia, during the 1984-2003 period, a total of 659 heart transplants have been performed on 648 patients (11 patients have had two transplants). In the year 2002, there were 50 first transplants performed and in the year 2003, 46 transplants and one re-transplant.

The annual evolution of the number of transplants has shown a growth tendency since the year 1992, coinciding with the authorisation of a new centre for providing this type of treatment, and it increased further from 1997 onwards, with the start-up of Catalonia's third transplant unit. It started to decrease from the year 2000 onwards, owing, amongst other factors, to a lack of organ availability and to the increase in pharmacological treatments for certain types of heart failure caused by dilated cardiomyopathy. In consequence, the annual transplant rate<sup>1</sup> has decreased in recent years: 7.7 per million population (pmp) in 2002 and 7.0 pmp in 2003 (figure 1).

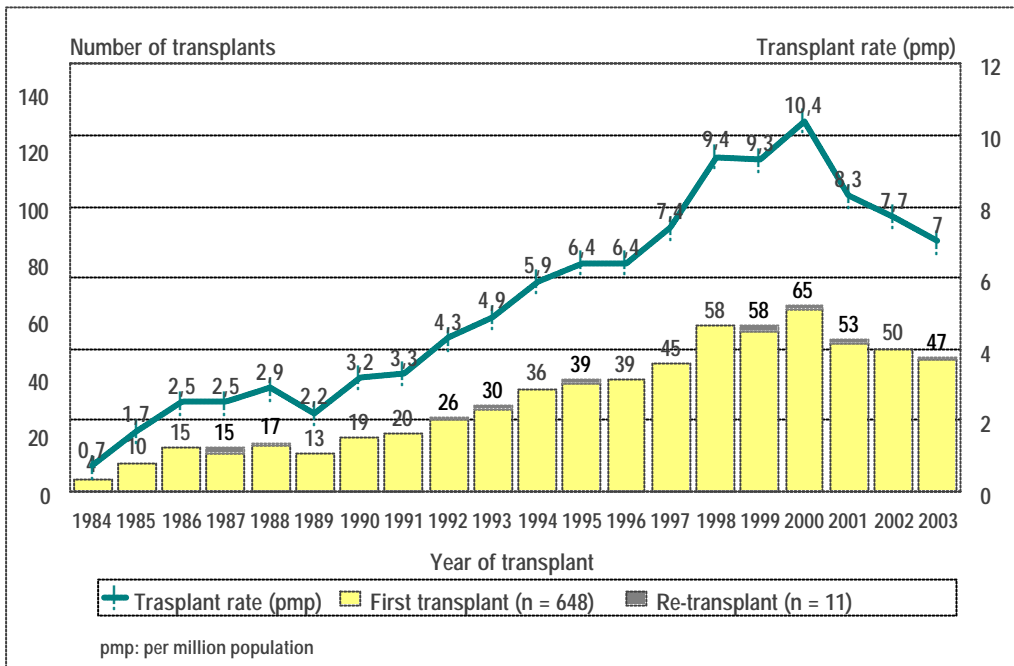
Even though this indicator varies considerably between countries, Catalonia ranks amongst the communities in our region with the highest amount of transplant activity (figure 2). In any event, these data must be interpreted with caution taking into account the different factors that influence transplant activity in each country (healthcare system, diagnostic indication, population structure, etc.).

Of the 648 patients included in the registry, 405 (62.5%) were still alive on 31 December 2003, 242 (37.3%) had died and one case (0.2%) was lost to follow-up.

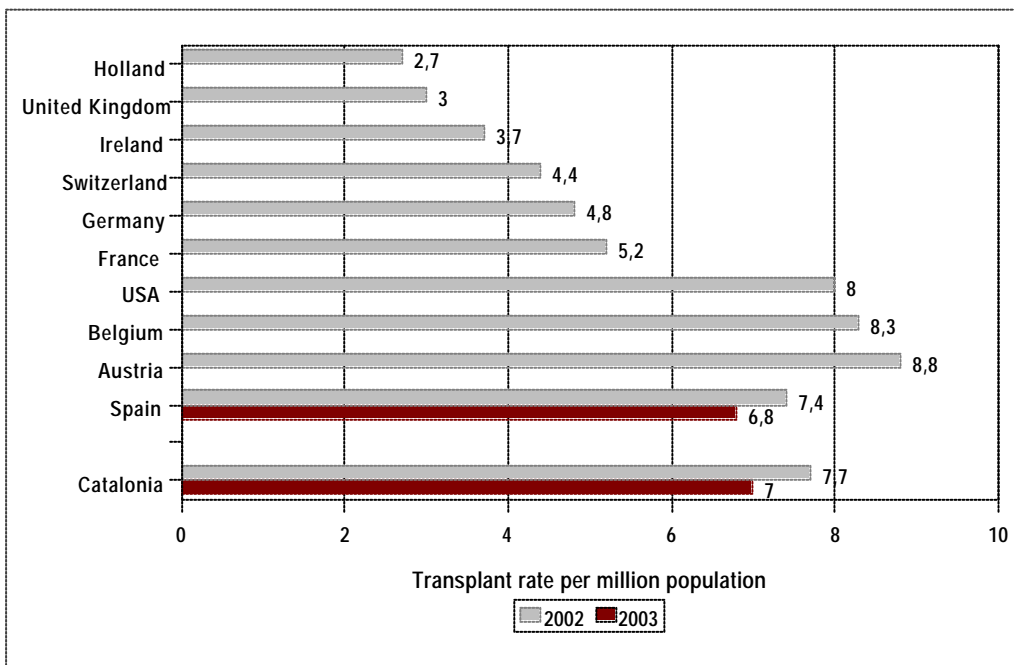
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<sup>1</sup> Total number of transplants carried out during the year at the authorised centres - independently of the place of residence of the recipient and of the origin of the donor - in relation with the population of Catalonia (Source: Catalan Statistics Institute and National Statistics Institute).

**Figure 1** Annual evolution of the number of transplants and the heart transplant rate. 1984-2003 period



**Figure 2** Heart transplant rate in different countries. Years 2002 and 2003



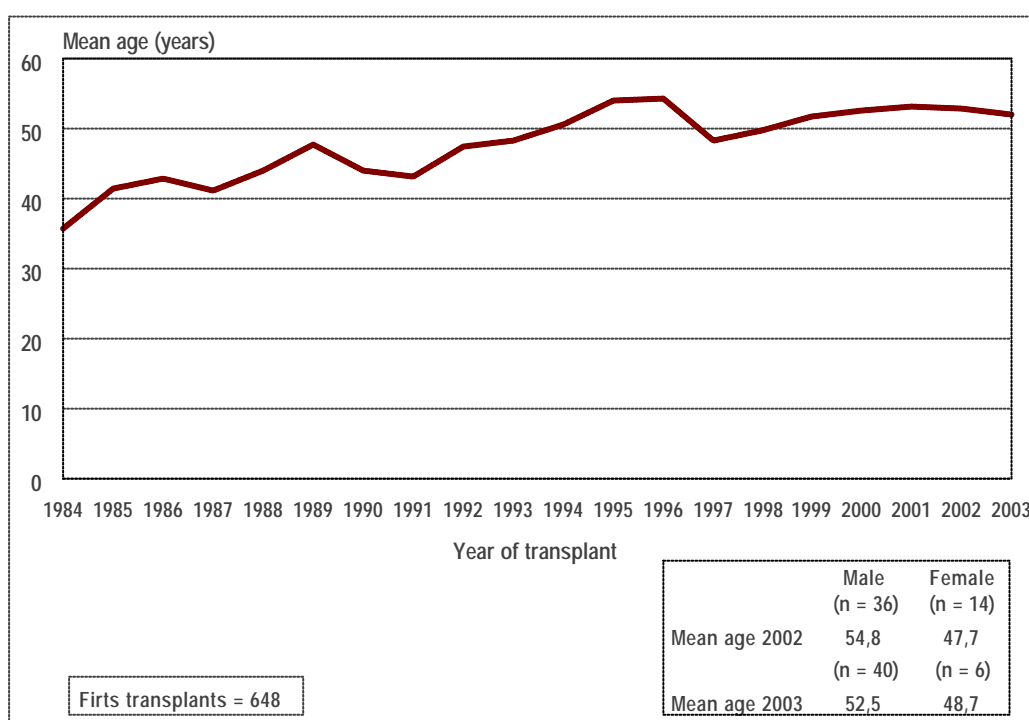
Sources: Catalan Statistics Institute (IDESCAT), Spanish National Transplants Organisation (ONT), European Council. International figures on organ donation and transplantation year 2002. *Newsletter Transplant 2003*; 8:9.

## Description of the population

Of the 648 patients that have had a heart transplant, 517 (79.8%) are men and 131 (20.2%) are women. This distribution is practically the same as for the 1984-2000 period.

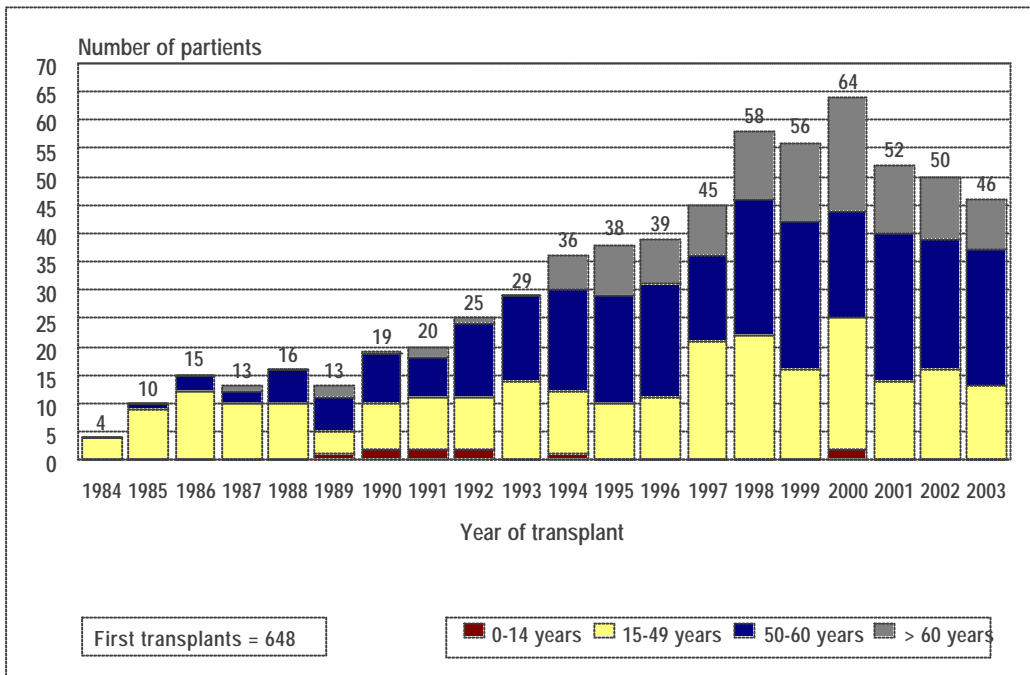
The mean average age for the entire set of patients is 50.0 years (50.4 for men and 48.3 for women), the median is 52.7 years and the range from 6 to 70 years. The global mean average age in the last two years has undergone a slight increase with respect to previous years: 52.8 years in 2002 (median: 52.2 years, range: 16-68 years) and 52.0 years (median: 53.6 years, range: 17-70 years) in 2003 (figure 3). The mean age of male patients is slightly higher than that of females. Given the low number of cases it must be taken into account that these data may be affected by extreme values.

**Figure 3** Annual evolution of the mean age of patients who have had a heart transplant. 1984-2001 period

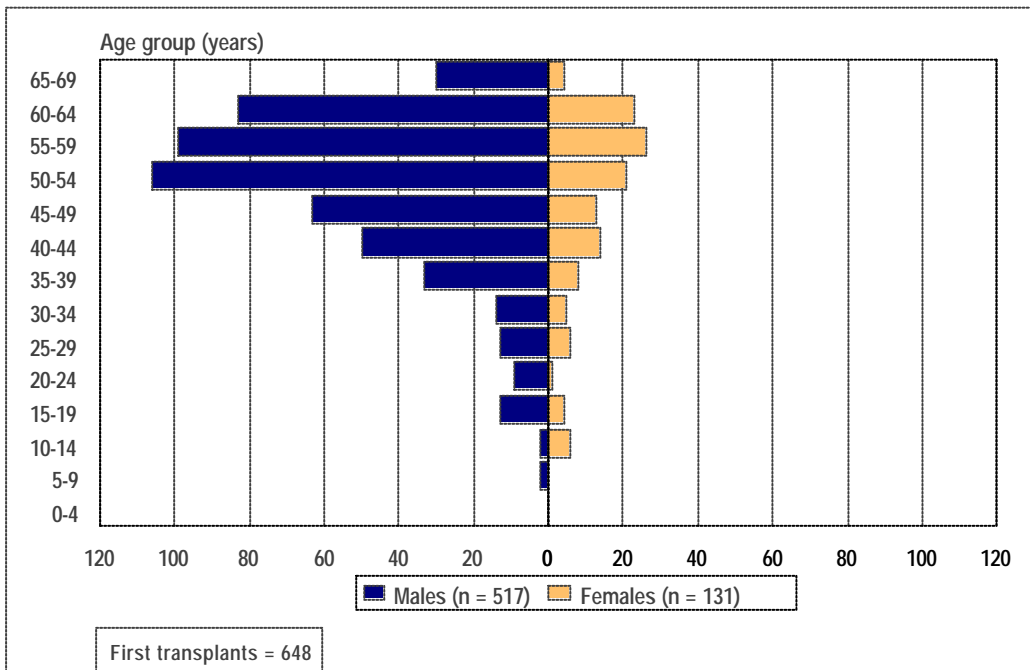


The increase in age observed over the years is mainly due to the progressive increase of transplants in patients aged over 50 years (figure 4). Patients aged between 35 and 64 years represent 83.2% of all heart transplants. Men aged between 50 and 64 years account for 55.7% of all the males and 44.4% of all the patients. There are 34 patients aged over 64 years (figure 5). The reduction in the number of transplants in the last three years in patients aged over 60 years coincides with the general reduction in the transplant rate.

**Figure 4** Annual evolution of the number of patients who have had a heart transplant, by age group. 1984-2003 period



**Figure 5** Number of patients who have had a heart transplant, by age group and sex. 1984-2003 period



Of the 648 patients who have had a heart transplant, 589 (90.9%) are resident in Catalonia, 59 (9.1%) elsewhere in Spain (mainly the Balearic Islands and Aragon) and one is resident abroad (0.1%). During the year 2002, transplants were received by 49 patients resident in Catalonia (98.0%) and one (2.0%) from Castilla-León. In the year 2003, 42 (91.3%) of patients were resident in Catalonia and four (8.7%) elsewhere in Spain.

The lowest crude cumulative incidence rate<sup>2</sup> correspond to the Lleida and Terres de l'Ebre healthcare regions, which are furthest away from the centres that perform heart transplants (table 1). It must be taken into account that, owing to the low number of patients from these regions, small variations in activity may substantially modify the rates.

In order to minimise the effect of confounding factors (demographic characteristics, such as age and gender) that can affect comparisons between different communities and Catalonia as a whole, the incident rates are standardised by age and gender in patients aged over 14 years. In the case of populations with a low frequency of the phenomenon to be analysed, indirect standardisation is used.<sup>3</sup> To reflect the current situation more precisely, this indicator is presented for the 1992-2003 period. In its calculation, the under-15 age group has been excluded owing to the low number of paediatric transplants (5) during this period.

**Table 1** Crude and standardised rates of cumulative incidence of first transplants in patients residing in Catalonia, by healthcare region where they live. 1992-2003 period

Healthcare region	Cumulative incidence			
	N	Crude rate pmp	Standardised rate pmp	CI 95%
Lleida	15	44,4	52,8	26,1-79,5
Tarragona	37	84,4	102,2	69,3-135,1
Terres de l'Ebre	4	30,0	34,9	0,7-69,0
Girona	48	92,4	111,5	80,0-143,1
Costa de Ponent	107	92,7	105,1	85,1-125,1
Barcelonès Nord and Maresme	50	72,8	85,3	61,6-108,9
Centre	102	78,0	91,8	73,7-109,9
City of Barcelona	143	94,8	106,6	89,0-124,1
<b>Total</b>	<b>506</b>	<b>83,1</b>	<b>96,4</b>	<b>-</b>

pmp: per million population.

CI 95%: confidence interval of 95%.

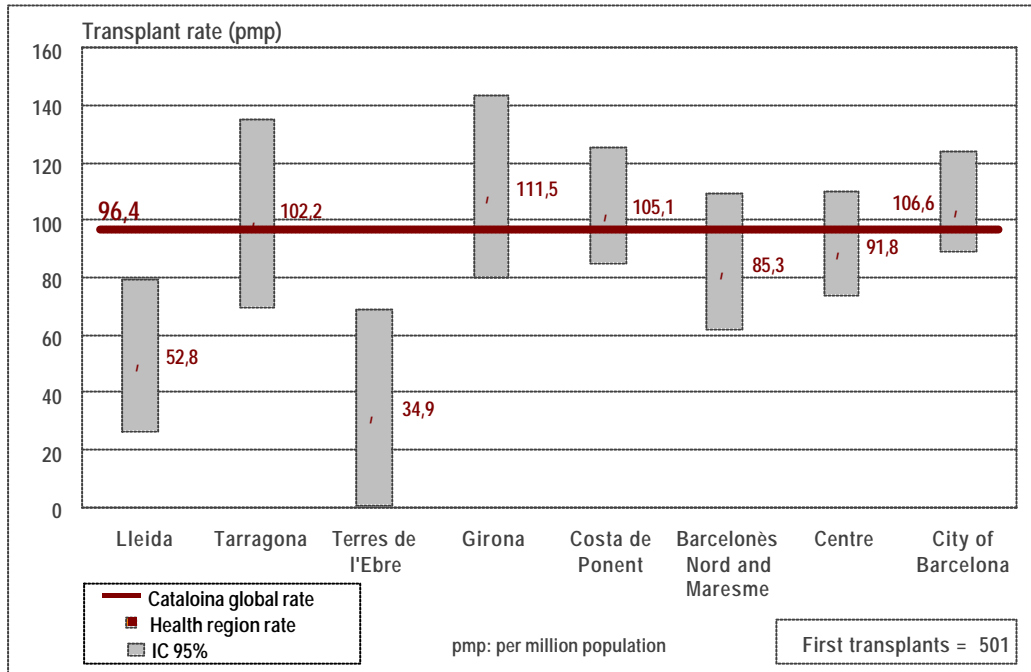
Thus, it can be observed that the standardised incidence rate in the majority of regions is situated around the global rate for Catalonia, and that those most distant from the rate continue to be Lleida and Terres de l'Ebre (figure 6). It must be taken into account that the confidence interval of the estimated rate is broader in regions with a lower number of cases. In the case of Tortosa, for example, the incidence rate lies between 0.6 and 59.7 pmp with a probability of

<sup>2</sup> Cumulative incidence: number of patients resident in Catalonia who received a first heart transplant during the period 1992-2003 (new cases), in relation with the population of each healthcare region and that of Catalonia (1996 Census of Inhabitants, Catalan Statistics Institute), per million population.

<sup>3</sup> Standardised cumulative incidence by age and gender, by the indirect method: this method consists of applying the specific incidence rates for each age group and gender of a standard or reference population to the same groups of populations under study, in this case, from the healthcare regions. The reference population used was the global population of Catalonia (1996 Census of Inhabitants, Catalan Statistics Institute). One of the limitations of this method is that it only allows the comparison of the rates of each region with that of Catalonia, but not between regions.

95%. The differences between the rates of these two regions and the global rate for Catalonia are statistically significant, because the confidence interval does not include the value of the Catalonia rate in either of the cases.

**Figure 6** Standardised cumulative incidence rate of first transplants in patients resident in Catalonia, by healthcare region where they live. 1992-2003 period



CI 95%: confidence interval of 95%.  
pmp: per million population.

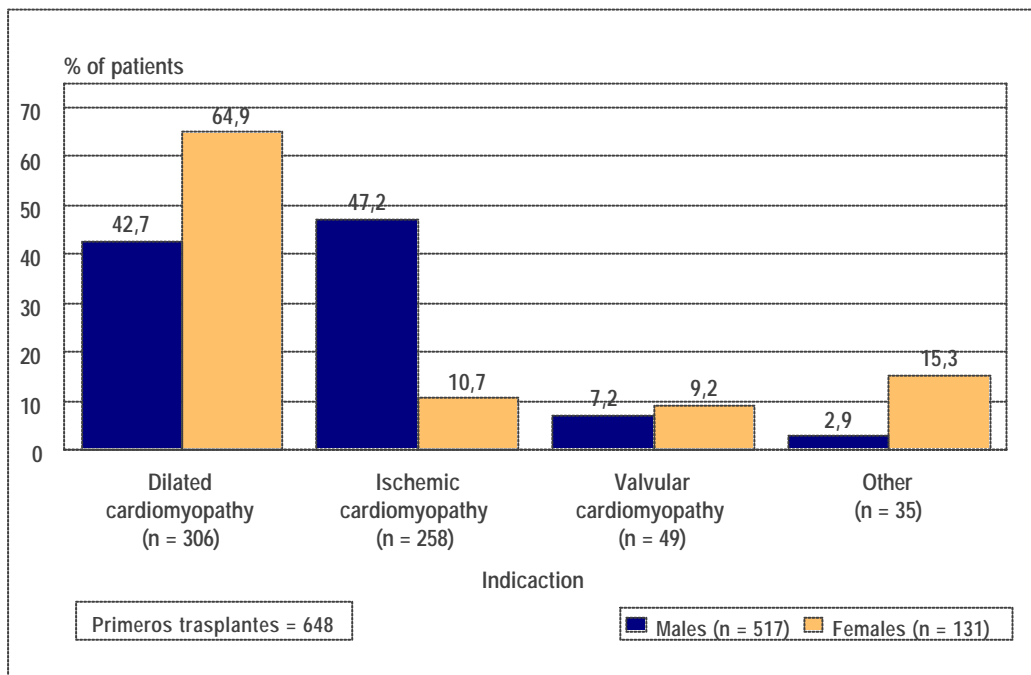
## Diagnostic Indication

The diagnostic indications for heart transplant of the patients included in the registry are grouped into the following categories:

- Dilated cardiomyopathy
- Ischemic cardiomyopathy
- Valvular cardiomyopathy
- Others (congenital cardiopathy, hypertrophic restrictive cardiomyopathy, etc.)

The most frequent diagnostic indication for heart transplant for the entire 1984-2003 period is dilated cardiomyopathy (47.2% of all patients), followed by ischemic cardiomyopathy (39.8%). In the case of men, the difference in the frequency of both indications is minimal. On the other hand, in women dilated cardiomyopathy represents 64.9% of all indications and ischemic cardiomyopathy represents just 10.7% (figure 7).

**Figure 7** Percentage of patients who have had a heart transplant, by diagnostic indication and gender. 1984-2001 period

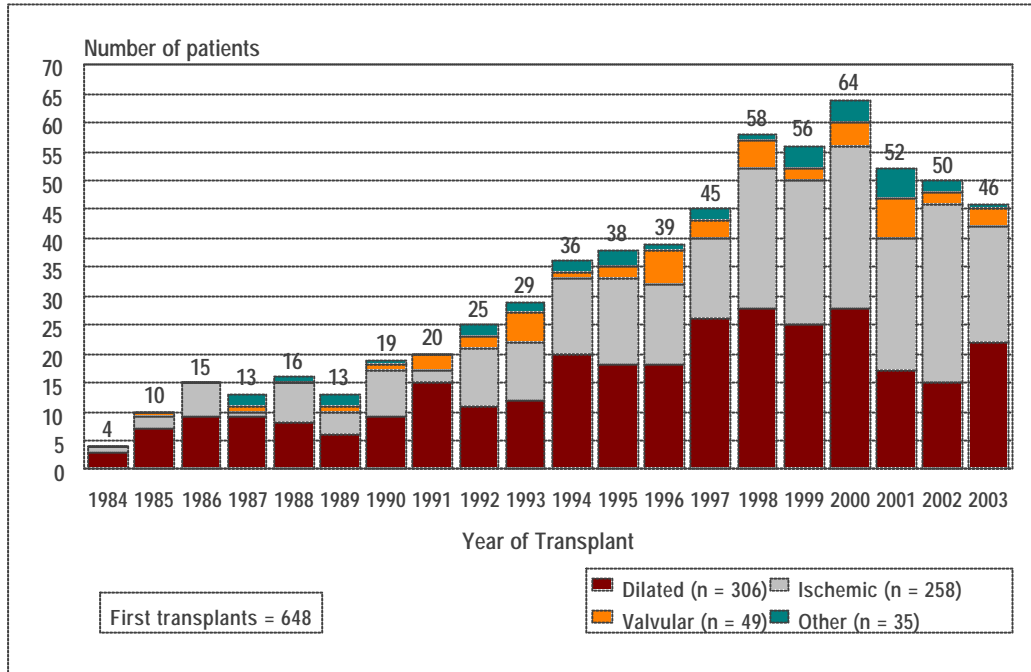


In any event, the annual evolution of the number of patients according to diagnostic indication shows that dilated cardiomyopathy was the most frequent indication up to the year 1998 and that ischemic cardiomyopathy has been increasing progressively in recent years, until in 2002 it became the most frequent indication (62% of all reasons). During the years 1999 and 2000, ischemic cardiomyopathy, which from 1997 onwards started to increase, represented the same percentage of indications as dilated cardiomyopathy. Although a growing tendency is observed of diagnostic indication owing to ischemic cardiomyopathy, the low number of transplants performed in recent years includes oscillations that are difficult to evaluate: in the year 2003, there were 22 transplants performed because of dilated cardiomyopathy, and 20 owing to ischemic cardiomyopathy (figures 8 and 9).

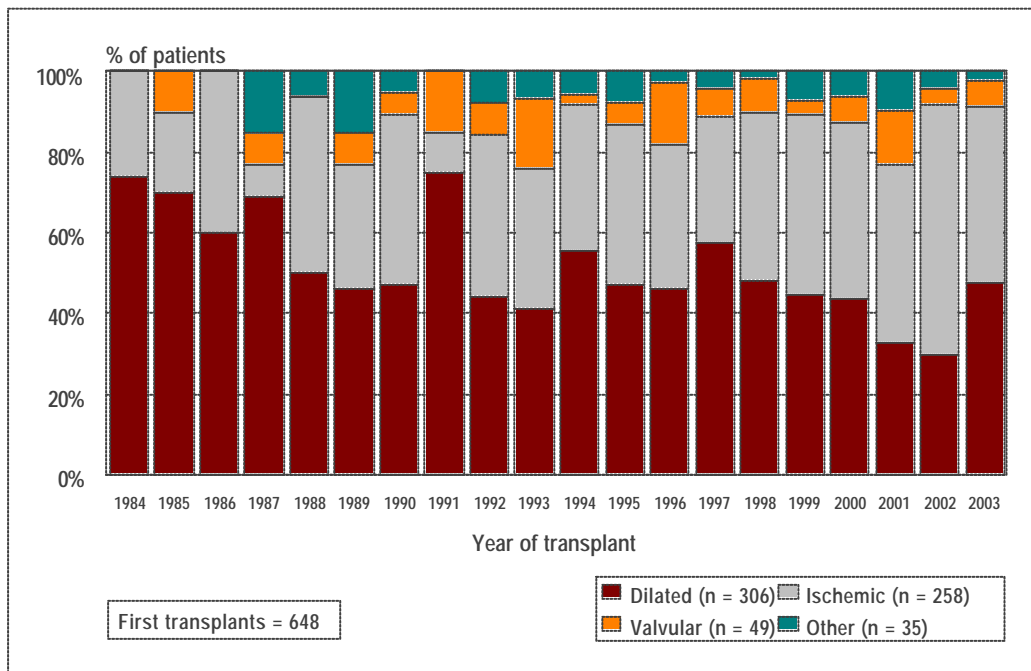
This fact can almost certainly be attributed, firstly, to the improvements achieved in the medical treatment of dilated cardiomyopathy and secondly, to a lack of organs owing to the care taken in the selection of donors in the case of heart transplants.

The annual evolution of patients with valvular cardiomyopathy or one of the cardiopathies from the “others” category is very heterogeneous owing to the low number that they represent.

**Figure 8** Annual evolution of the number of patients who have had a heart transplant, per diagnostic indication. 1984-2003 period



**Figure 9** Annual evolution of the percentage of patients who have had a heart transplant, per diagnostic indication. 1984-2003 period



The mean age presents statistically significant differences ( $p < 0.0001$ ) between the different diagnostic indications: in general patients with ischemic or valvular cardiomyopathy are older than those suffering from dilated cardiomyopathy (table 2).

These differences are maintained when this variable is analysed separately amongst men ( $p < 0.0001$ ) and amongst women ( $p < 0.0001$ ).

**Table 2** Mean age by indication and gender. 1984-2003 period

Diagnostic indication	N	Mean age (years)		
		Male O <sup>1</sup> (CI 95%) <sup>2</sup>	Female O <sup>1</sup> (CI 95%) <sup>2</sup>	Total O <sup>1</sup> (CI 95%) <sup>2</sup>
Dilated cardiomyopathy	306	46,6 (44,7-48,5)	50,4 (47,7-53,1)	47,7 (46,1-49,2)
Ischemic cardiomyopathy	258	54,1 (53,2-55,0)	51,9 (47,1-56,7)	54,0 (53,1-54,9)
Valvular cardiomyopathy	49	54,3 (51,5-57,1)	51,0 (43,6-58,4)	53,5 (50,8-56,1)
Other cardiopathies	35	37,4 (27,7-47,1)	35,0 (26,8-43,2)	36,1 (30,1-42,0)
<b>Total</b>	<b>648</b>	<b>50,4 (49,4-51,5)</b>	<b>48,6 (45,8-51,7)</b>	<b>50,0 (49,0-50,9)</b>

<sup>1</sup>O: mean age in years.

<sup>2</sup>CI 95%: confidence interval of 95%.

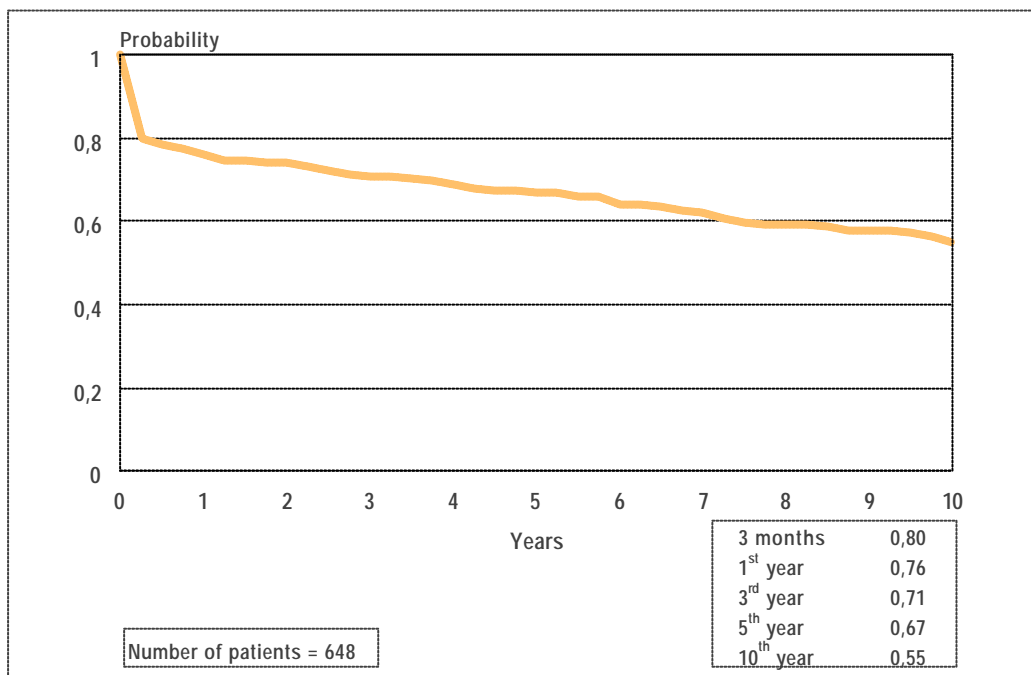
## Survival

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The actuarial method was used to calculate the survival rate of patients who have had a heart transplant and the level of statistical significance between the different curves was evaluated using the Wilcoxon (Gehan) test. The survival curves were interrupted when the number of cases fell below 10.

When studying the global survival rate during the 1984-2003 period, it can be seen that patients who have had a heart transplant have a survival probability of 76% at the end of the first year, of 71% at the end of the third year, of 67% at the end of the fifth year and of 55% at the end of tenth year (figure 10).

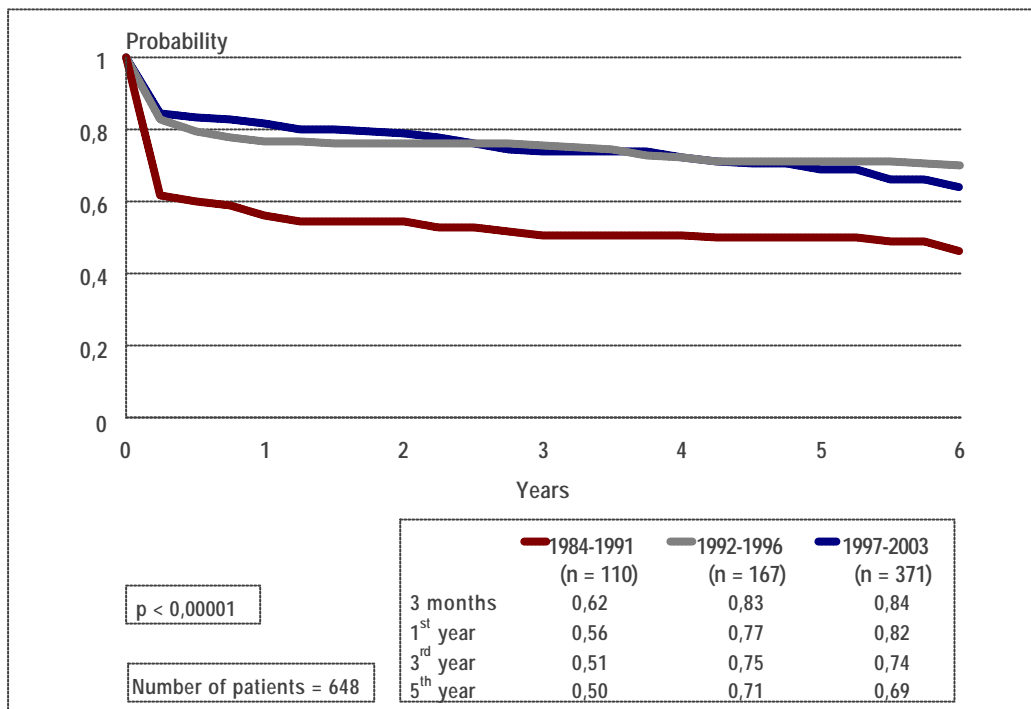
**Figure 10** Survival of patients who have had a heart transplant. 1984-2003 period



It must be taken into account that the global survival rate is affected both by the characteristics of the transplants carried out during the first years (low number of cases, learning period), as well as by other factors related with transplants carried out in later years (inclusion of patients with conditions of more serious prognosis and of an older age).

So that the results are adjusted as far as possible to the context of each phase, three periods have been defined to analyse the survival rate (figure 11). Thus, differences are observed between the three periods, although between the second and the third period they are not statistically significant.

**Figure 11** Survival of patients who have had a heart transplant, by periods. 1984-2003 period



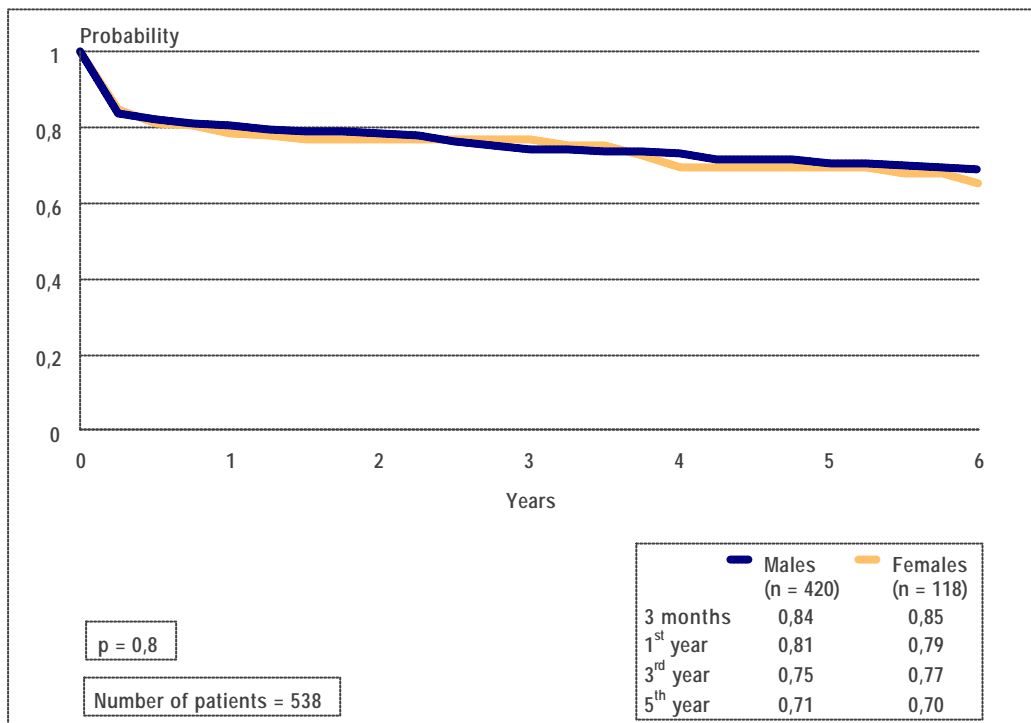
The different survival analyses that are presented below have been calculated with the data on transplants performed since 1992, given that the current behaviour of heart transplants is much closer to the pattern of survival observed in the last two periods.

The survival of patients according to gender does not present highly significant differences ( $p = 0.8$ ), although men have a slightly higher survival rate than women (figure 12).

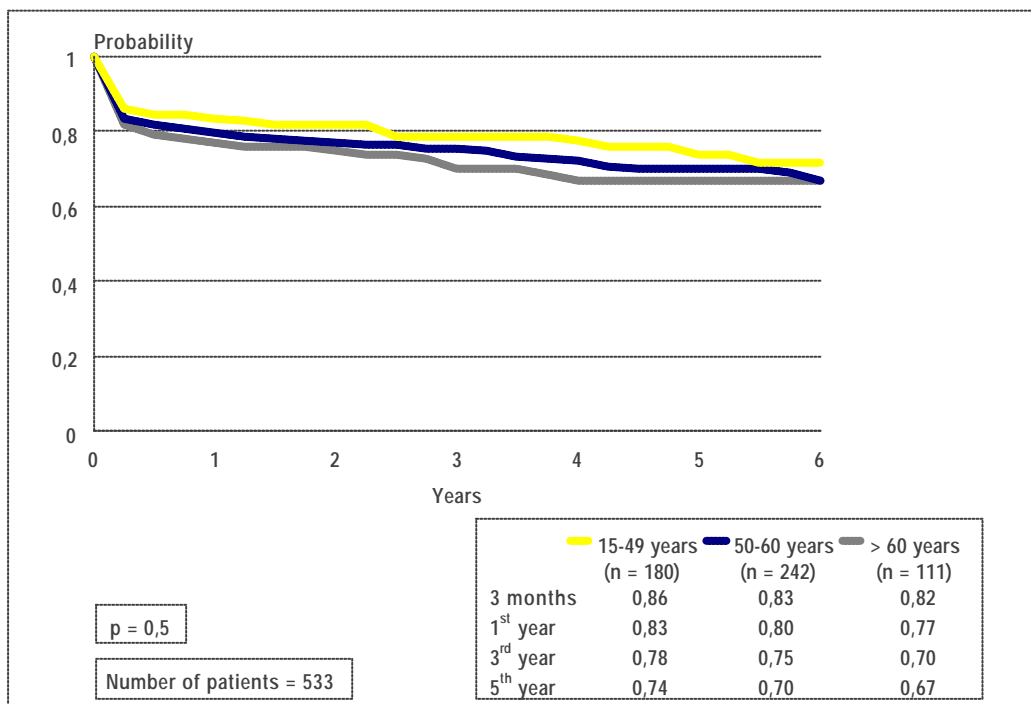
Given the low number of patients aged under 15 years (five cases) that have had a transplant since the year 1992, this group has not been included in the analysis of survival by age.

The group of patients aged between 15 and 49 years has a better survival rate than that of patients in the 50 to 60 years age group, and that of the over 60 years age group, although this difference is not statistically significant if this group is compared with the others ( $p = 0.3$  and  $p = 0.2$ , respectively). The greatest difference between groups (8%) is observed in the three year survival rate between patients aged 15 to 49 years and patients aged over 60 years (figure 13).

**Figure 12** Survival of patients that have had a heart transplant, by gender. 1992-2003 period

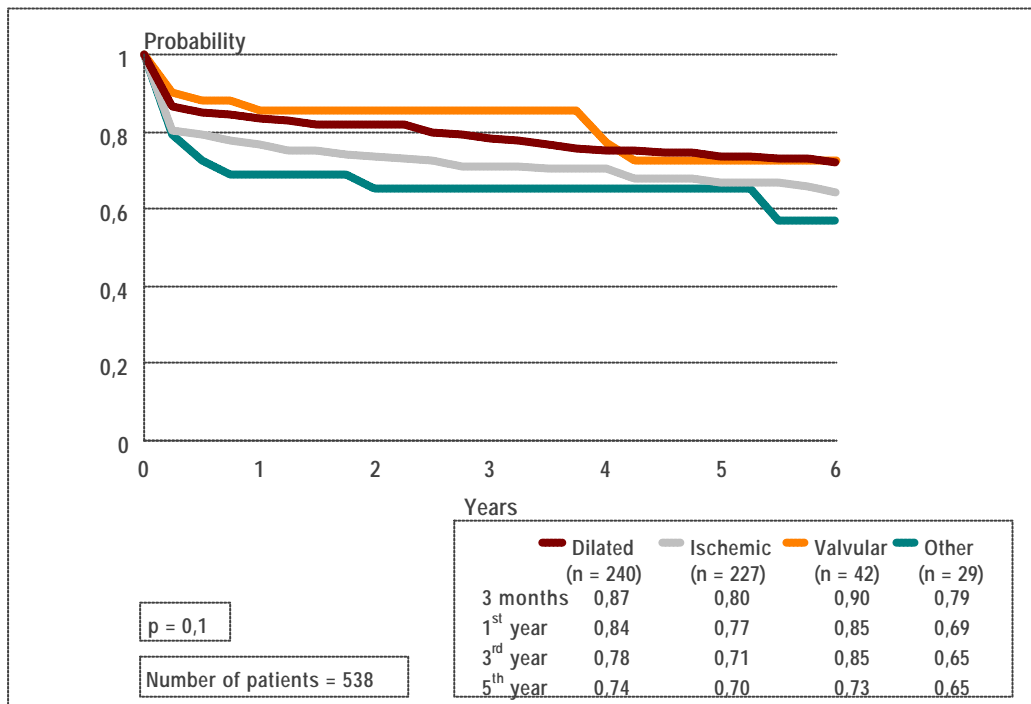


**Figure 13** Survival of patients aged over 14 years who have had a heart transplant, by age group. 1992-2003 period



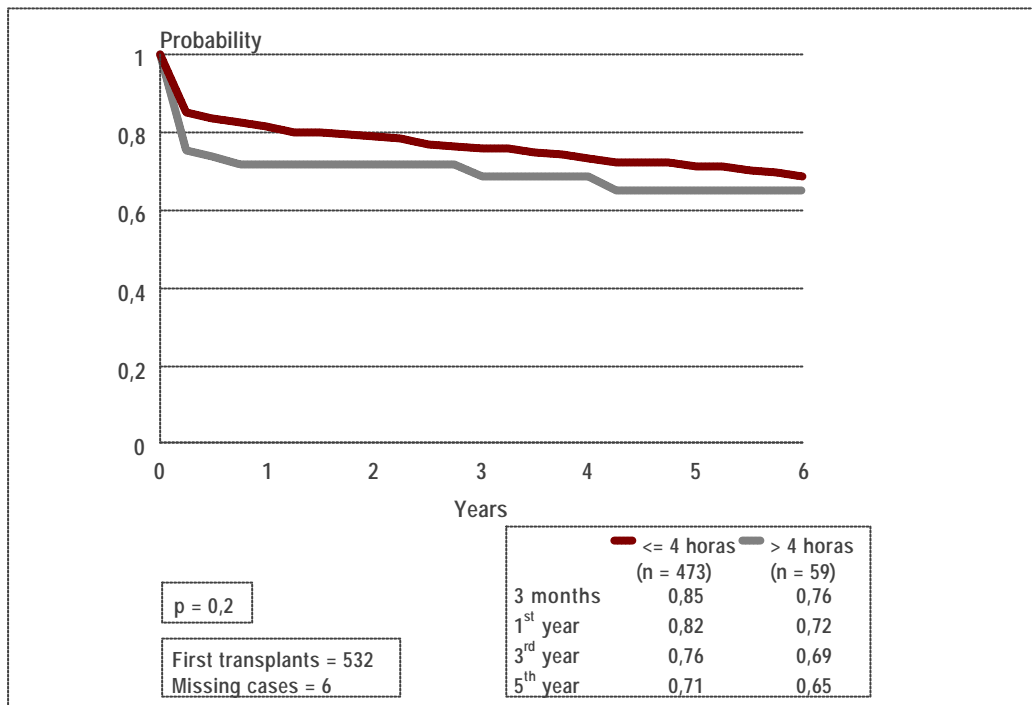
The differences in survival rates of patients according to diagnostic indication are not statistically significant ( $p = 0.1$ ). Although at three months, patients who have suffered from valvular cardiomyopathy present the best survival rates, patients with dilated cardiomyopathy are those who have a higher probability of survival in the long term (figure 14). When comparing survival rates between patients with dilated cardiomyopathy and those who suffer from ischemic cardiomyopathy, the differences observed (around 7% in the first three months, after one year and after three years, and around 4% in the fifth year) are at the limits of statistical significance ( $p = 0.07$ ).

**Figure 14** Survival of patients who have had a heart transplant, by diagnostic indication. 1992-2003 period



When survival is analysed according to the time that has passed between extraction of the organ to the moment of transplant, it is observed that probability is greater when cold ischemia time is less than or equal to four hours, although the differences are not statistically significant ( $p = 0.2$ ) (figure 15). The most important differences are those evident in the short term (9% at three months and 10% at one year).

**Figure 15** Survival rate of patients who have had a heart transplant, according to cold ischemia time. 1992-2003 period

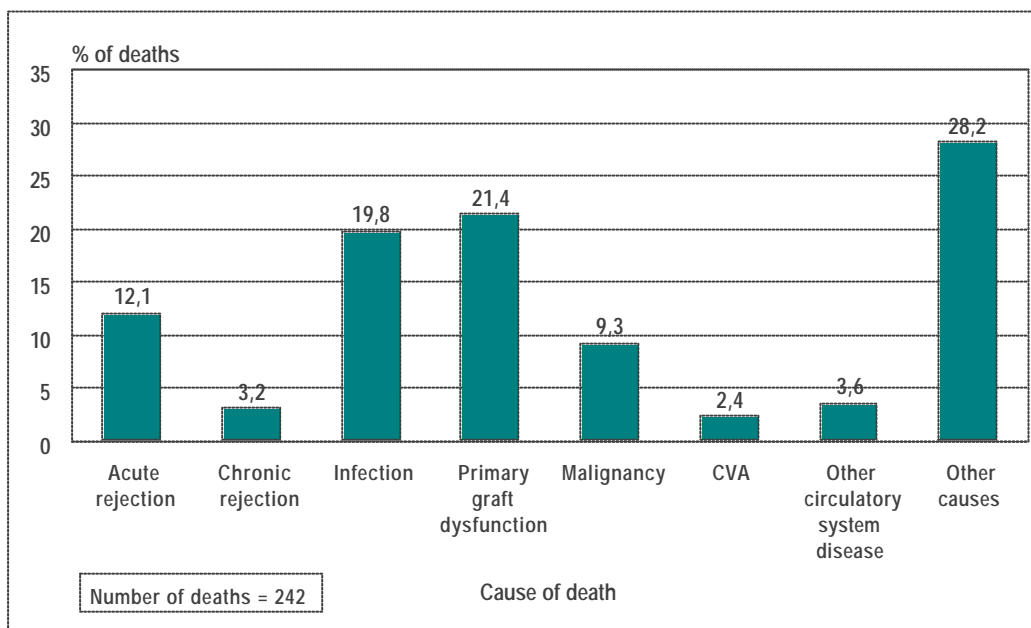


## Mortality

Of all those patients who had a transplant during the 1984-2003 period, 242 have died: 196 men and 46 women (37.9% of men and 35.1% of women), which represents a global mortality rate<sup>4</sup> of 37.3%.

The most frequent causes of death are primary graft dysfunction (21.5%), infections (19.4%) and acute rejection (12.4%) (figure 16). These three causes are the reason for 55.3% of all deaths. The most frequent cause of death in the “others” category is sudden death (15 cases).

**Figure 16** Percentage of deaths according to the cause of death. 1984-2003 period

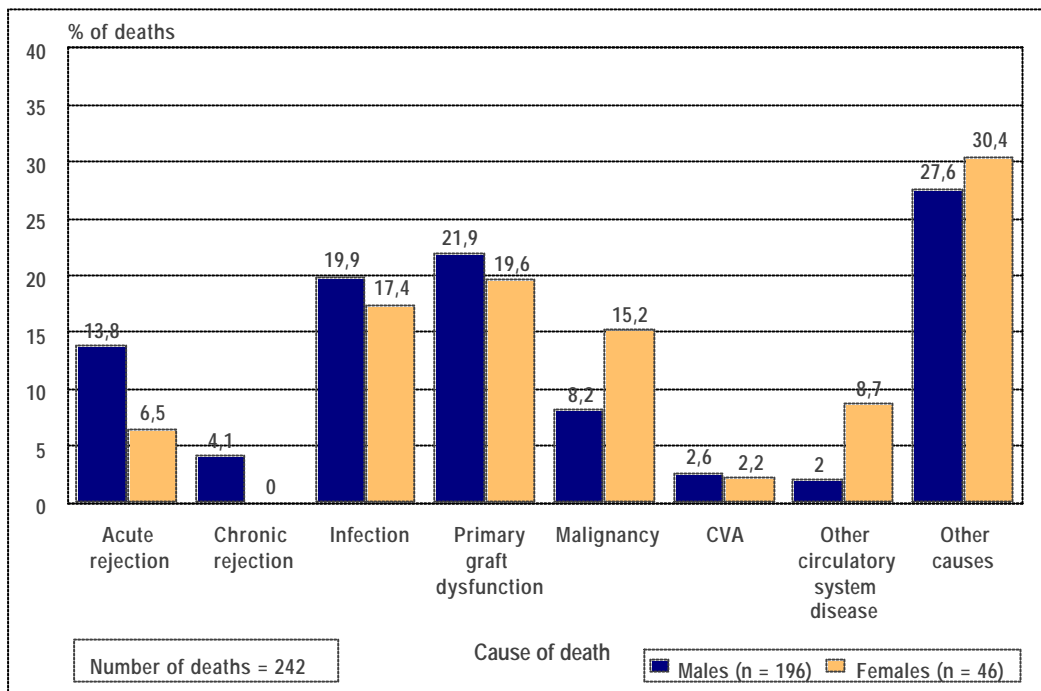


In men the top three causes of death are the same as for the entire population of patients, whereas in women, the third most frequent cause is malignancy instead of acute rejection (figure 17). In any case, the differences that can be observed between sexes cannot be evaluated owing to the low number of deaths corresponding to women (46 in the entire period).

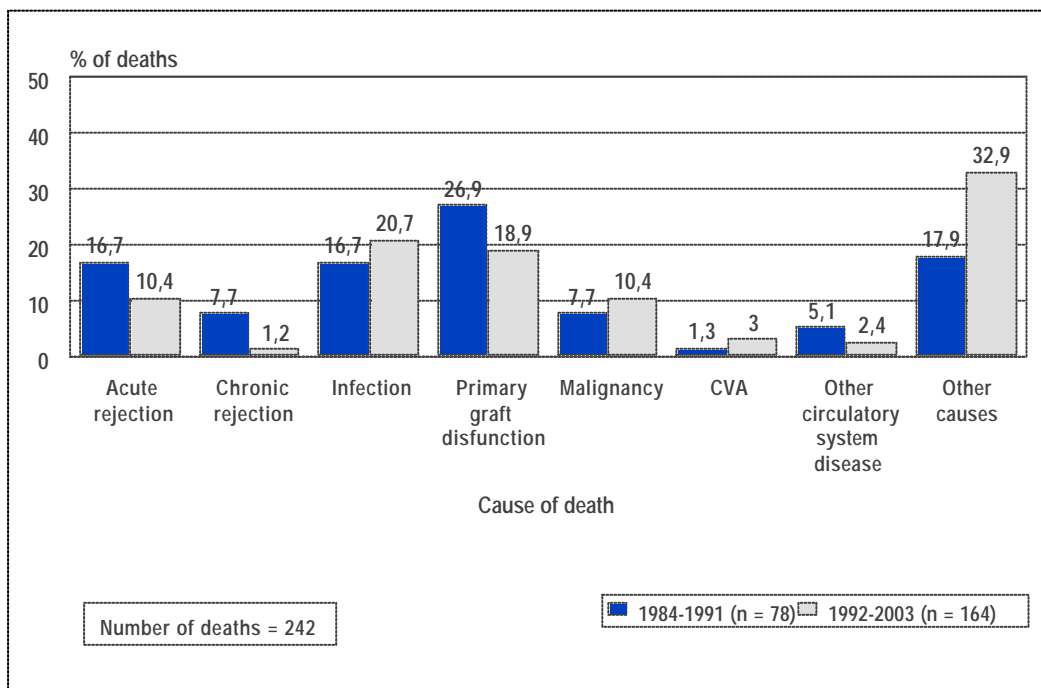
When studying the causes of mortality by period, it is confirmed that the percentage of deaths owing to primary graft dysfunction and to chronic rejection has decreased, but there is an increase in those owing to infections and malignancy (figure 18). This change in the evolution of the reasons of death could be related to the use of new immunosuppressors that avoid rejection but favour the appearance of related illnesses that affect the immune system.

<sup>4</sup> Global mortality: percentage of deaths that have occurred at any time, during a determined period of time, in the population of patients that have had a heart transplant.

**Figure 17** Percentage of deaths, according to cause of death and gender. 1984-2003 period



**Figure 18** Percentage of deaths by cause of death and period. 1984-2003 period



For the early mortality study, the mortality rate during the first 30 days subsequent to transplant is used. This indicator describes the mortality related with the technique or with other factors such as the diagnostic indication.

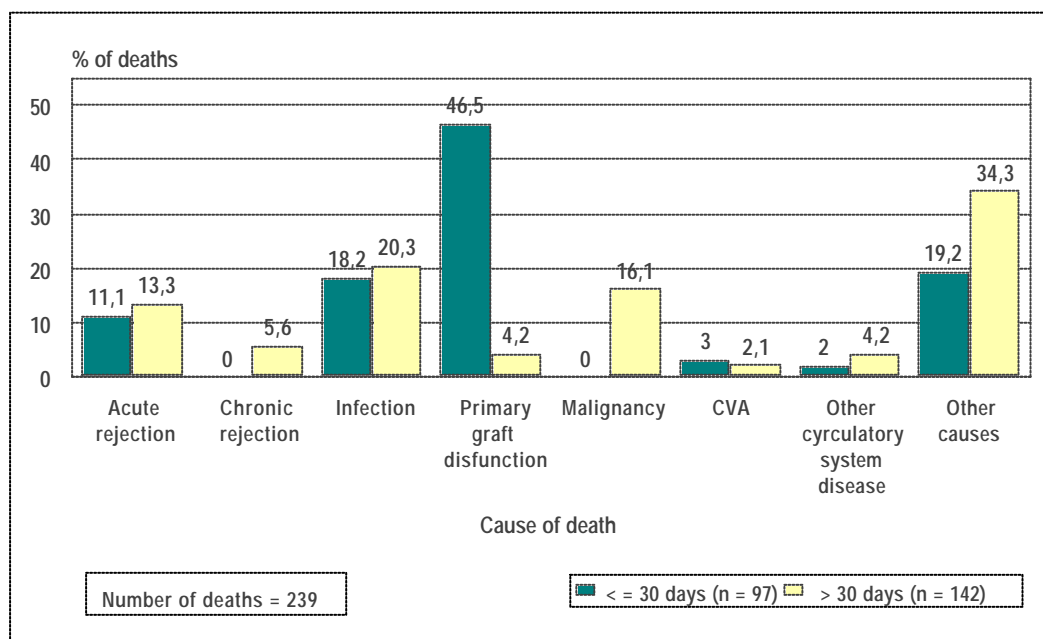
Since the closing date for the mortality and survival analysis is 31 December 2003, the early mortality rate is calculated for the 1984-2002 period, since in the case of patients who had the transplant towards the end of the month of December 2003, it is not known whether they died in the first 30 days following the transplant.

Of the 239 patients that have died during the 1984-2002 period, 97 (40.1%) did so during the 30 days following the transplant. During 1984-1996 period 227 first transplants were performed and 53 deaths took place within the first month after transplant, which represents a 30-day mortality rate<sup>5</sup> of 19.1%. This rate decreased in the most recent period (1997-2002) to 13.5%, with 325 transplants performed and 44 deaths observed during the firsts 30 days.

Some 17.4% of men and 11.2% of women who had a first transplant during this period died during the 30 days following the transplant.

Some 65% of the deaths occurring in the first 30 days subsequent to transplant are due to primary graft dysfunction and to infections (figure 19); in the group of patients that have died after the first 30 days, the most frequent causes of death are infection, neoplasia and acute rejection, without taking into account the “others” category. The three causes mentioned account for 49.3% of all deaths occurring after 30 days.

**Figure 19** Cause of death of recipient, according to the time that has passed since the transplant. 1984-2002 period

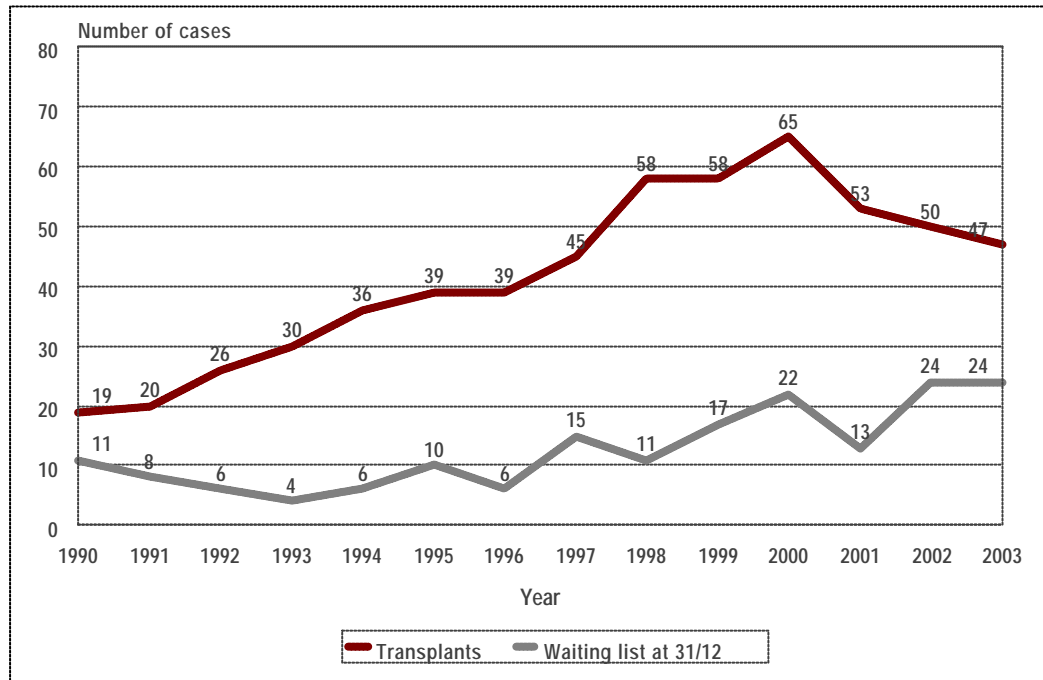


<sup>5</sup> 30-day mortality rate: percentage of deaths occurring within the 30 days subsequent to transplant in the population of patients that have had a heart transplant.

## Waiting list

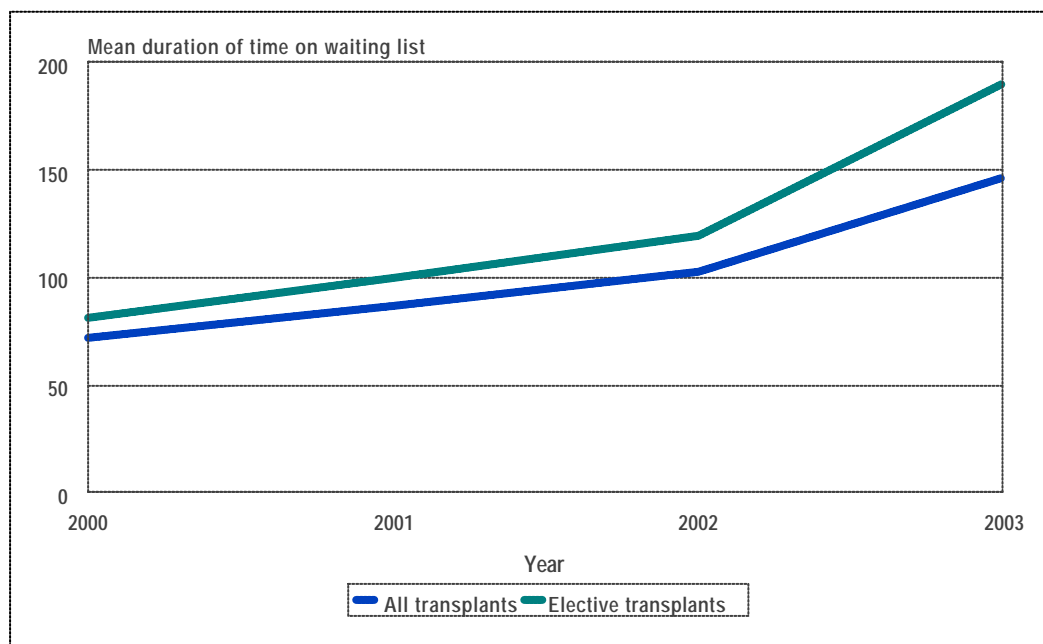
Although the number of heart transplants has decreased in recent years, there is a growing trend in the number of patients on the waiting list (figure 20).

**Figure 20** Evolution of the waiting list and of the number of heart transplants. 1990-2003 period



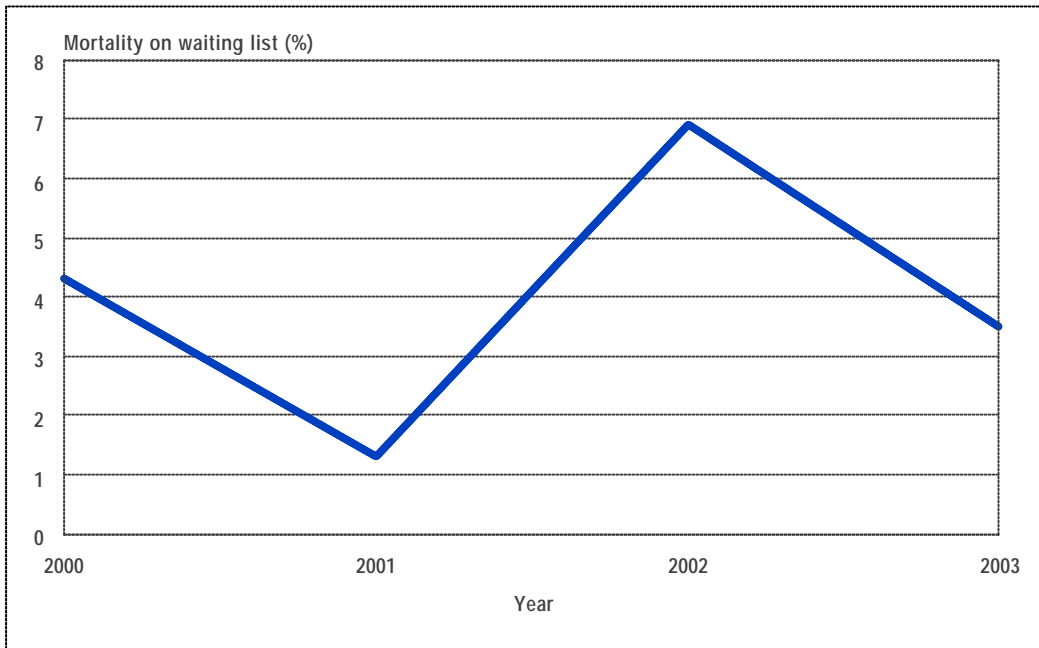
The mean duration on waiting list for a heart transplant was 103 days in the year 2002 and 146 days in 2003. If emergency transplants are excluded from the calculation, these figures rise to 119 and 190 days respectively (figure 21).

**Figure 21** Mean duration of time on heart transplant waiting list. 2000-2003 period



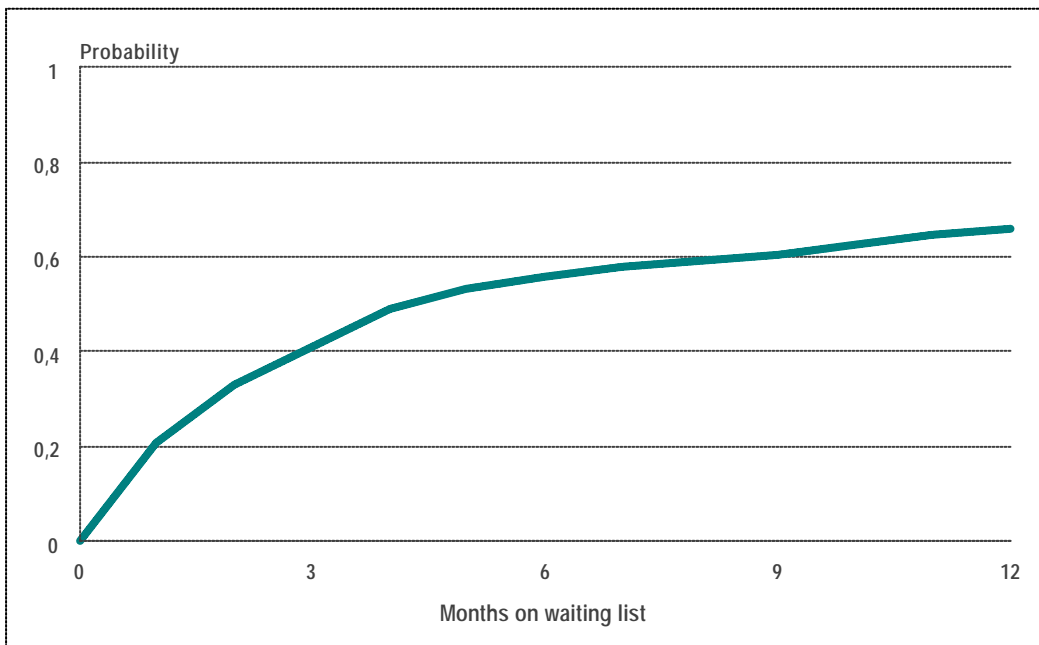
During the year 2002, there were 83 new inclusions in the list and 74 during the year 2003. The majority of withdrawals were due to the worsening of the patient's condition. The mortality rate on the waiting list was 6.9% in the year 2002 and 3.5% in the year 2003. Owing to the low number of cases in recent years, the considerable fluctuations that are observed must be evaluated with caution (figure 22).

**Figure 22** Mortality percentage on the waiting list to receive a heart transplant. 2000-2003 period



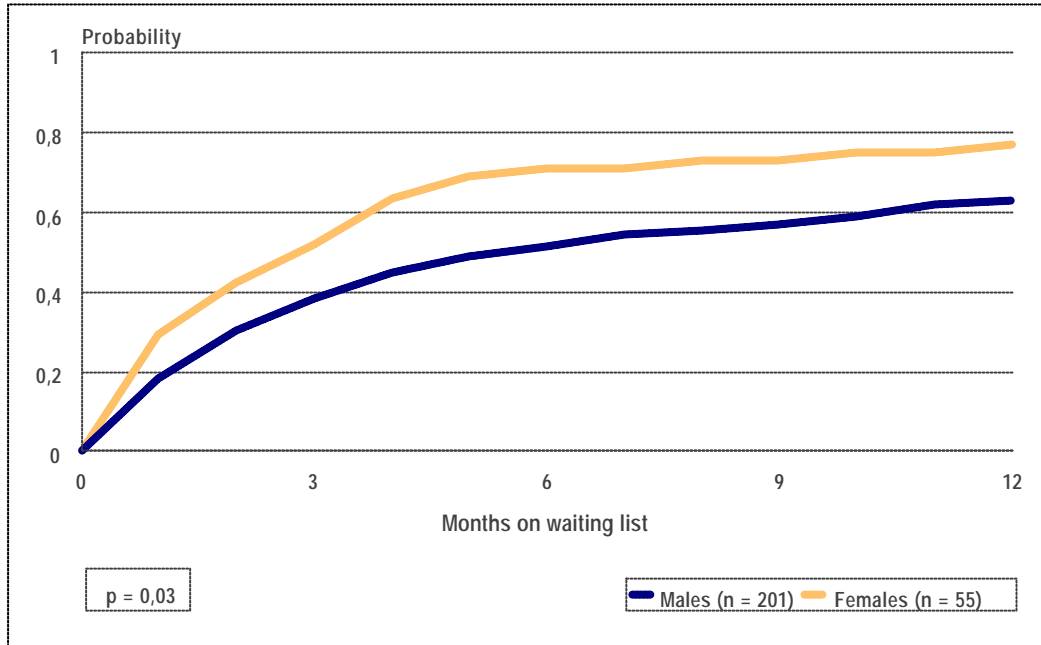
During the 2000-2003 period, the probability of receiving a heart transplant was of 56% after six months on the waiting list and of 66% after one year (figure 23).

**Figure 23** Probability of receiving a heart transplant 2000-2003



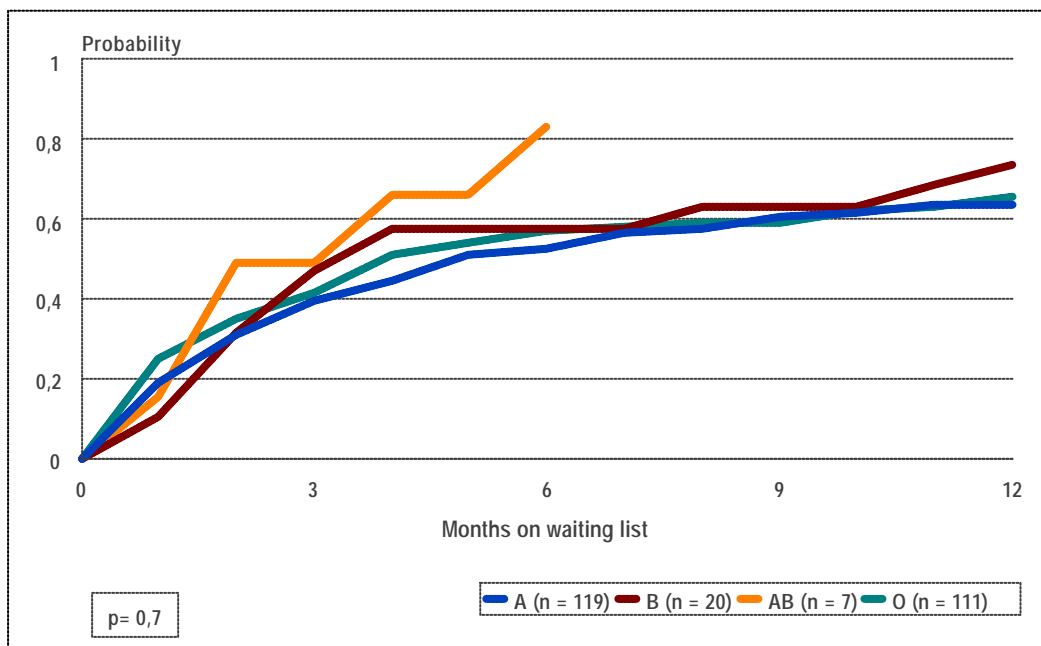
When the probability of receiving a transplant is analysed according to the gender of the patient, it is observed that in women the probability (71.1% at six months and 77.2 at one year) is higher than in men (51.5% at six months and 63.0% at one year). These differences are statistically significant ( $p = 0.03$ ) (figure 24).

**Figure 24** Probability of receiving a heart transplant, by gender. 2000-2003 period



Although recipients with the AB blood group have the highest probabilities of receiving a transplant, the differences that are observed between this and the other groups are not statistically significant ( $p = 0.7$ ) (figure 25).

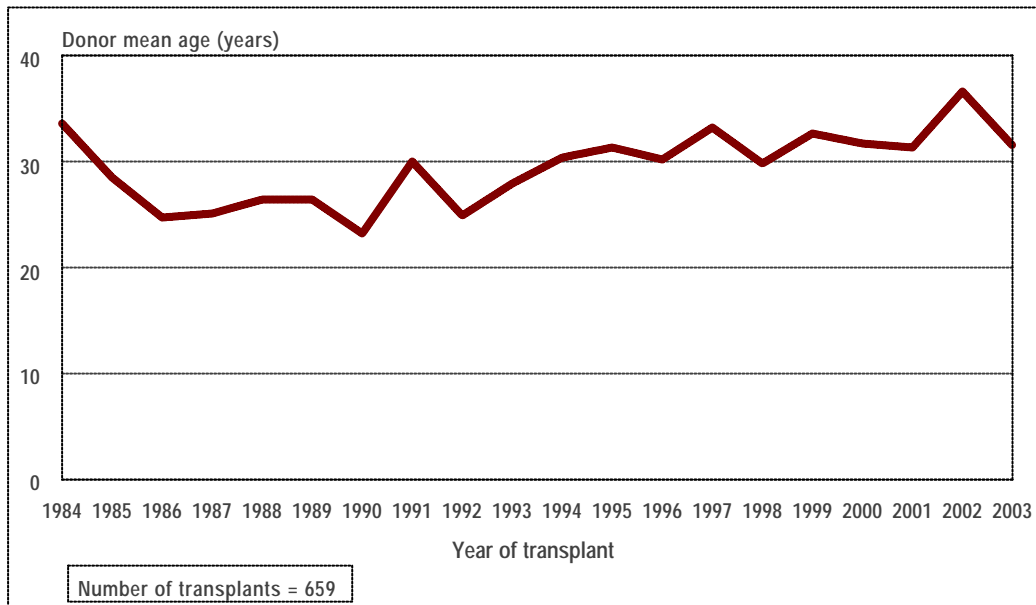
**Figure 25** Probability of receiving a heart transplant, by blood group. 2000-2003 period



## Donation data

With respect to the age of the donor, a slight increase in the yearly mean age is observed over the entire period, although the low number of cases during the first few years must be taken into account. The global mean age is 30.5 years (range: 5-59) (figure 26).

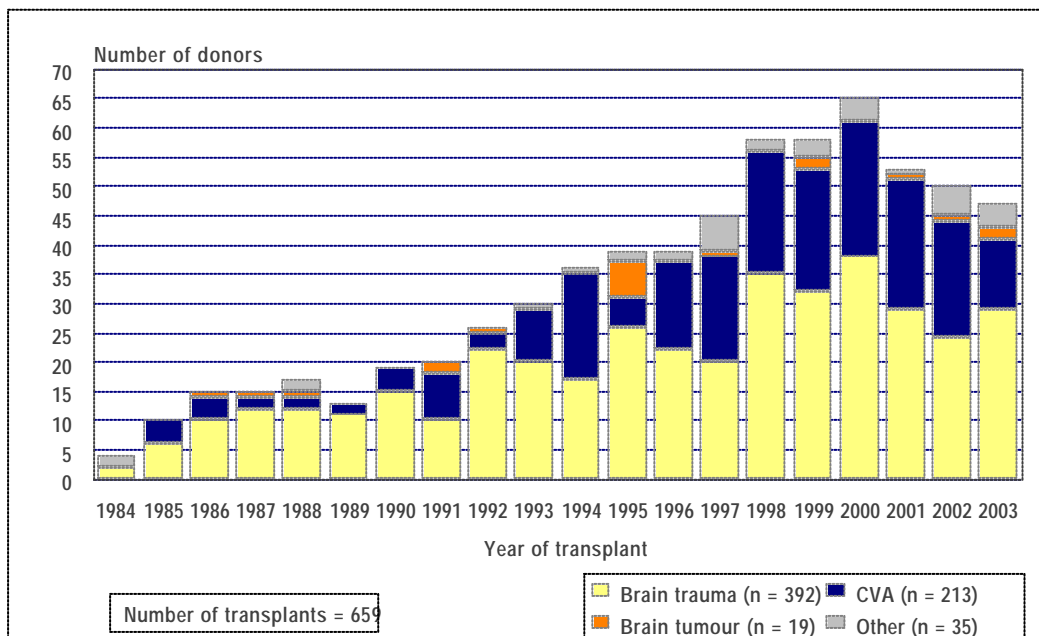
**Figure 26** Mean age of donor. 1984-2003 period



71.9% of donors are men and 28.1% are women. In 140 cases (21.2%) there is a lack of information on this variable. In the year 2003, 39 of the 47 donors were men and eight were women.

The most frequent cause of death of the donor is head trauma (59.5% of all the causes) (figure 27).

**Figure 27** Annual evolution of donor cause of death. 1984-2003 period



22.8% (150) of the hearts transplanted came from the same hospital in which the transplant was performed, with 46.4% (306) from other hospitals in Catalonia and 30.8% (203) from hospitals outside Catalonia (table 3).

The mean age of donors does not show any differences according to the place of origin of the organ ( $p = 0.9$ ).

When analysing mean cold ischemia time according to the place of origin of the organ, the differences observed are statistically significant ( $p < 0.0001$ ). When the organ comes from a centre outside Catalonia, the mean time is 75.6 minutes higher than when the organ is obtained from a hospital in Catalonia.

As regards the cause of death of the donor, statistically significant differences are not observed ( $p = 0.4$ ).

**Table 3** Specific data on transplants, on the organs transplanted, and the donors, according to the place of origin of the organ. 1984-2003 period

Age of donor (years)	Same hospital (n = 150)	Rest of Catalonia (n = 306)	Outside Catalonia (n = 203)	Total (N = 659)
Mean	30,6	30,7	30,3	30,5
Median	28,0	29,0	29,0	28,0
Range	10-59	12-57	5-58	5-59
IC 95%	28,7-32,4	29,4-32,0	28,7-31,8	29,7-31,4
Cold ischemia time (minutes)	Same hospital (n = 147)	Rest of Catalonia (n = 301)	Outside Catalonia (n = 199)	Total (N = 647*)
Mean	127,4	144,1	219,7	163,6
Median	125,0	140,0	220,0	154,0
Range	60-230	25-275	69-360	25-360
IC 95%	122,5-132,3	139,5-148,7	213,8-225,6	159,4-167,8
Cause of death of donor	Same hospital (n = 150)	Rest of Catalonia (n = 306)	Outside Catalonia (n = 203)	Total (N = 659)
Head trauma	60,0 %	59,2 %	59,6 %	59,5 %
CVA	32,0 %	32,0 %	33,0 %	32,3 %
Brain tumour	2,0 %	4,6 %	1,0 %	2,9 %
Others	6,0 %	4,2 %	6,4 %	5,3 %

\* In 12 cases information on the cold ischemia time is missing.

## Re-transplants

Of the 659 transplants performed during the 1984-2003 period, 11 were re-transplants. The majority of these were performed on men (table 4). The most frequent diagnostic indication was dilated cardiomyopathy, followed by ischemic cardiomyopathy.

When studying graft survival, it is observed that in five cases the re-transplant took place between six and thirteen years after the first transplant, whilst in the remaining six cases the graft duration was between two months and two days.

Of these 11 cases, six have died: two owing to infection, one from primary graft dysfunction, one owing to a circulatory system disease and two from other causes.

The characteristics of the donors involved do not differ from the rest of the heart donors.

**Table 4** Characteristics of re-transplants. 1984-2003 period

Characteristics of recipient	
Gender	
Male	8
Female	3
Age (years)	
Mean	43,2
Median	43,1
Range	22-64
Indicating diagnosis	
Dilated cardiomyopathy	6
Ischemic cardiomyopathy	4
Hypertrophic cardiomyopathy	1
Characteristics of transplant	
Ischemia time *	
Mean	127,4
Median	125,0
Range	60-230
CI 95%	122,5-132,3
Characteristics of donor	
Age (years)	
Mean	33,6
Median	33,0
Range	18-51
Cause of death	
Head trauma	8
CVA	1
Brain tumour	1
Others	1

\* In three cases, information on the cold ischemia time is missing.

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