

Figure 2. Kidney waiting list Spain.

balance between the annual needs and the transplant procedures.

In our country the rate of cadaver kidney transplant raised during the last years up to an average of 50 pmp. So, the patients in waiting list decreased during the early nineties till keeping stabilised, and recently showing a swift trend to increase (fig. 2)

It can be said that the Spanish donation and transplantation rate has been enough to cover the demand during some years but not exactly now. Moreover, the historic accumulate of patients in kidney waiting list makes that this global figure of waiting list doesn't decrease below 4000 patients.

These data, although don't satisfy us complete, however place Spain in a privilege situation in relation to others countries. In USA, for example, the kidney waiting list had recorded less than 18,000 patients during 1990; while ten years later are more than 50,000, the patients included. The kidney transplants have increased in USA, especially for the living transplant activity, but less than the waiting list. [2]

Also in the European Space the living donation has increased and contributed to the overall increase in transplant figures. However, more than 46,000 patients are waiting for a kidney transplant at this moment [3]

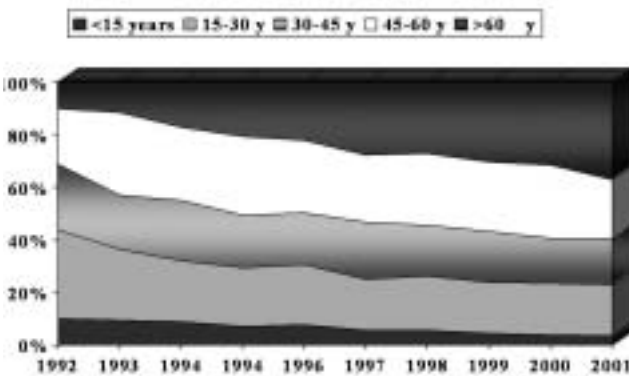


Figure 4a. Organ donor Spain 2001 age groups.

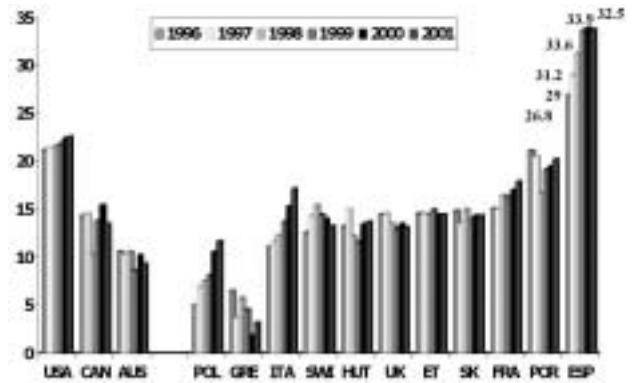


Figure 3. Organ donor Rates.

This generalised problem of misbalance between the transplant necessities and the shortage of organs for transplant has changed the attitude of the transplant teams during the last years. Trying to reduce these differences, the criteria for accepting donors has been expanded. In these moment very young or aged donors, donors with positive viral markers or asystolic donors are considered as real donors bearing in mind some specific requirements during the evaluation process of each donor. [4]

Evolution of the Donation in Spain

Since 1990 and after the establishment of a complete donation and organ procurement infrastructure [5], the number of donors has increased progressively up to 1991, being the stabilised (Fig 3). The donor profile has been changing along this time, as has been described elsewhere [6]

Mean age has increased by ten years average and now, more than 33% of our donors are over 60 years, and 11% over 70 years. During 1992 these percentages were absolutely different as more than half of the donors were less than 45 years old (fig 4). Currently, the main cause of death among our donors is stroke, road traffic accidents account for not more than 21% of all donor's deaths (fig 5). The percentage of multiorgan donors, whose extra renal organs are retrieved, has increased during the last years, being

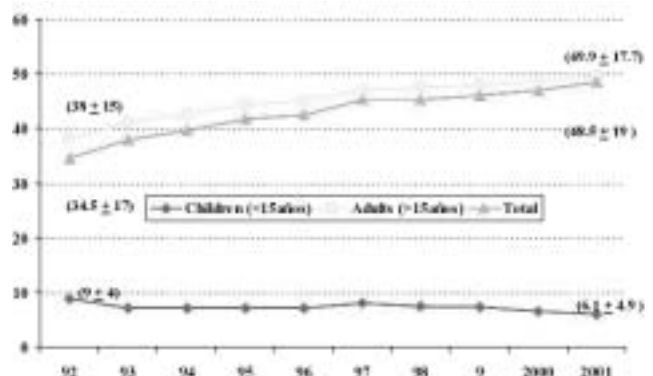


Figure 4b. Organ donor Spain 2001 mean age.

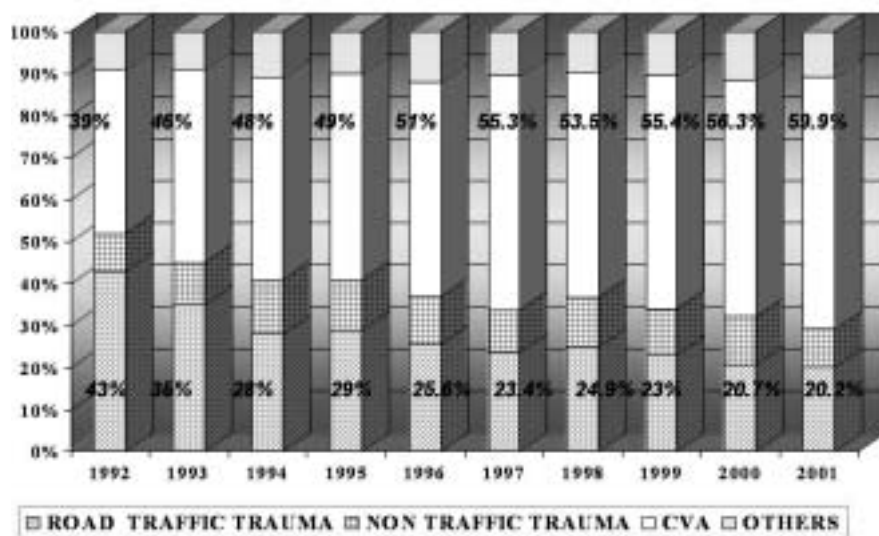


Figure 5. Organ donors Spain 2001 causes of brain death.

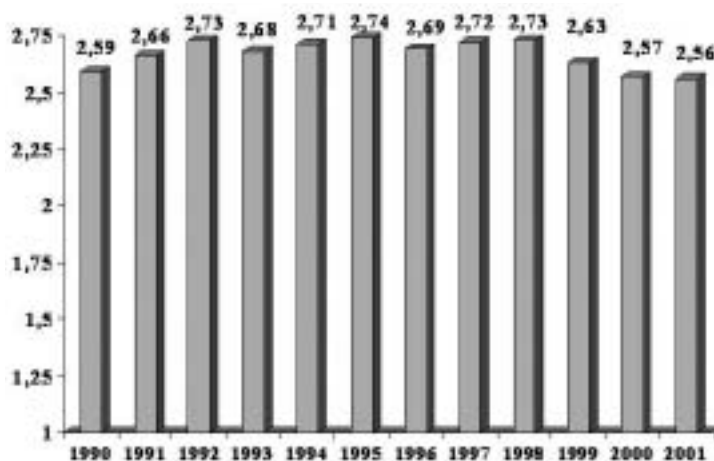


Figure 6. Transplanted organs per each donor Spain 1990-2001.

now more than 80%. However, the older are the donors, the more organs are discarded. Five years ago we grafted 2.8 organs per donor and nowadays only 2,5 organs per donor are effectively grafted. (Fig 6).

Donors Whose Organs are Rejected for Transplantation.

Within the general pool of donors there is always a percentage that are transferred to the surgical theatre and from whom are retrieved solid organs that afterwards cannot be used. Table 1 specifies absolute figures and rates representing all these data. Effective donation means that at least one solid organ has been grafted being a kidney or any other solid organ

In many cases final result was foreseeable, but it must be stated that there are also many doubtful cases and cases without any point for suspicion. There are also many donors with a high degree of suspicion for not being valid and whose organs were grafted. All this justifying the evaluation of all people with brain death and no major contraindications as potential donors,

not rejecting anyone prior to the final evaluation before the open body.

The rejecting causes range from the technical problems during the retrieval to the existence of a tumour or the unfitness to find the suitable recipient, as it has been published previously. [6]. Kidney rejection causes corresponding to 2001 are specified in table 2. We've recorded the cause of rejection in all the 567 kidneys that were not suitable for transplantation during last year. In all cases the corresponding report from the Pathology Department was available

As has been stated, in the cases of effective donation, not only are the kidneys the grafted organs. Table 3 shows how in several cases kidneys cannot be used but other organs are grafted. Table 4 shows the characteristics of these donors.

Table 5 specifies the characteristics of the donors depending on the number of kidneys used or discarded. Finally table 6 specifies the number and rates of discarded kidneys depending on the donor age.

Table 1. Organ donors, efficient organ donors and kidneys retrieved/grafted in Spain

	1998	1999	2000	2001
Million Population	39.6	39.6	39.6	45.2
Organ Donors (OD)	1250	1334	1345	1335
Efficient OD	1162	1217	1214	1200
Organ Donors pmp	31.5	33.1	33.9	325
Efficient OD pmp	29.3	30.7	30.6	29.2
Kidneys Retrieved	2431	2587	2550	2517
Kidneys Grafted	2016	2049	1982	1950
Kidneys Discarded	415	538	568	567

Table 2. Causes for Kidney Rejection (2001)

	N°	(%)
	240	42.3
Previous Kidney dysfunction	2	
Sepsis – Fungal infection – HIV	12	
Hypertension or Diabetes	18	
Aortic Aneurysm or Kidney artery Aneurysm	24	
Donor related causes		
Unconfirmed malignancy. (Suspicion)	24	
Confirmed malignancy after retrieval	46	
Virus B, C combined with aging or absence of euglycemic recipient	47	
Atherosclerosis – Arteriosclerosis	67	
Organ or retrieval process related causes	311	54.8
Horseshoe Kidney	4	
Lithiasis/Hydronephrosis	7	
Decepsulation	8	
Hypoplasia/Agenesis	13	
Trauma	16	
Vascular problems	22	
Pyelonephritis	24	
Technical problems/(Vascular/Ureteric)	28	
Multiple Cystis/Policystic disease	43	
Bed perfusion/Thrombosis	53	
Glomerulosclerosis/Interstitial fibrosis	93	
Recipient related causes	16	2.8
Cross match + and/Overpassed I Time	12	
Recipient vascular problems	4	

Table 3. Donors whose Kidneys were not used but from whom other organs were grafted

	1999	2000	2001
Heart	8	17	12
Lung	6	4	7
Liver	111	133	141
Small Bowell (pediatric)	–	1	–

Table 4. Characteristics of Table 3 donors

	Age	Cause Death (%)			Hypert.(%)		Diabet (%)		N
		Trauma	Stroke	Other	Yes	No	Yes	No	
Lung									
1999	46 ± 10	–	83	10	60	40	–	100	6
2000	36 ± 23	–	75	25	50	50	–	100	4
2001	38 ± 19	14	86	–	43	57	29	71	7
Heart									
1999	33 ± 23	–	88	12	29	71	17	83	8
2000	33 ± 16	41	47	12	15	85	–	100	17
2001	25 ± 22	25	58	17	22	78	13	88	12
Liver									
1999	62 ± 15	14	78	7	61	39	24	76	111
2000	60 ± 18	15	74	11	53	47	25	75	133
2001	61 ± 18	13	77	10	59	41	30	70	144

Sometimes the positive serologic test can affect the possibility of grafting a given organ. With increasing frequency it becomes more difficult to find a positive recipient fitting the donor profile. From 1993 to 1995, 75% of the generated kidneys with positive serologic test to virus C were grafted, nowadays this percentage is around 50%. From the 25 virus C donors of 1999 were grafted 26 kidneys and from the 27 virus C donors of 2000 were grafted 34 kidneys. Relating to the HB virus, from the six donors of 1999 were performed four kidney transplants and from the 13 of 2000, only 15 transplants were performed

Figure 6 shows the evolution of the virus C or B or CMV prevalence among our donors.

Discussion

It becomes very clear that donor profile has shown an important change during last years. Advances in the knowledge of better preservation techniques, different grafting techniques, better and more effective immunosuppression therapeutics did allow this evolution, although some changes in patient or graft survival have been observed. On the other hand and

simultaneously, recipient admission criteria has also shown an enormous change [7,8] It is hence difficult to state if the results with the so called “suboptimal” donors are so far from the results obtained with “optimal” donors. First of all threshold between both optimal and suboptimal is not so well established. Moreover, there are some factors related with both the process itself and the recipient’s characteristics that also have some impact on the graft outcome such as age, clinical circumstances, primary disease, immunosuppressive therapy, centre experience etc. Several authors have described less survival, increased morbidity and higher costs when several risk factors are combined in the same transplant process [4] It becomes mandatory to find the exact middle point between the number of transplants and its quality, moreover when speaking about kidney transplantation and hence having other alternatives. Kidney transplant gives to the kidney patients higher levels of perceived quality of life [9] Nevertheless, the use of organs from elderly donors or from donors with some pathological antecedents can raise ethical questions. [10] Are the patients ready to accept those “marginal” organs?

Table 5. Donor characteristics depending on the number of kidneys used or discarded

	Kidneys Used								
	NONE			ONE			TWO		
	1999	2000	2001	1999	2000	2001	1999	2000	2001
Number	197	275	281	159	159	153	933	911	899
Non Heart Beating	8	8	6	4	6	–	20	18	12
Age	60.8 ± 15	58 ± 19	61 ± 17	51.3 ± 19	51 ± 19	53 ± 19	42 ± 18	43 ± 18	44 ± 18
Cause of death (%)									
Trauma	15	17	14	23	32	24	40	36	36
Stroke	74	69	76	66	57	68	49	53	54
Other	11	14	10	11	11	8	11	11	10
Hypertension (%)									
Yes	58	51	58	41	39	40	21	25	25
No	42	49	42	59	61	60	79	75	75
Diabetes (%)									
Yes	18	26	28	12	14	8	6	6	5
No	72	74	72	88	86	92	94	94	95

Recently this question was offered to patients admitted in a kidney centre where the average waiting time was one year. Up to 70% of them would accept an organ of “inferior” quality if this implies less waiting

time [10]. It remains very difficult to say what will be the limit.

We have studied the evolution of the characteristics of our donors as well as the characteristics of the rejected

Table 6. Kidneys grafted and discarded depending on the age group

Age (Years)	< 15	15-29	30-44	45-59	60-69	>70
1999						
Grafted	85	492	445	545	349	111
Discarded	5	22	50	142	155	146
(%) Disc	5.5%	4.3%	10.1%	20.8%	30.7%	56.8%
2000						
Grafted	67	476	371	574	348	108
Discarded	9	45	68	156	134	155
(%) Disc	11.8%	8.6%	15.5%	21.4%	28%	59%
2001						
Grafted	58	441	395	608	311	134
Discarded	16	25	51	91	206	176
(%) Disc	21.6%	5.4%	11.4%	13%	39.8%	56.8%

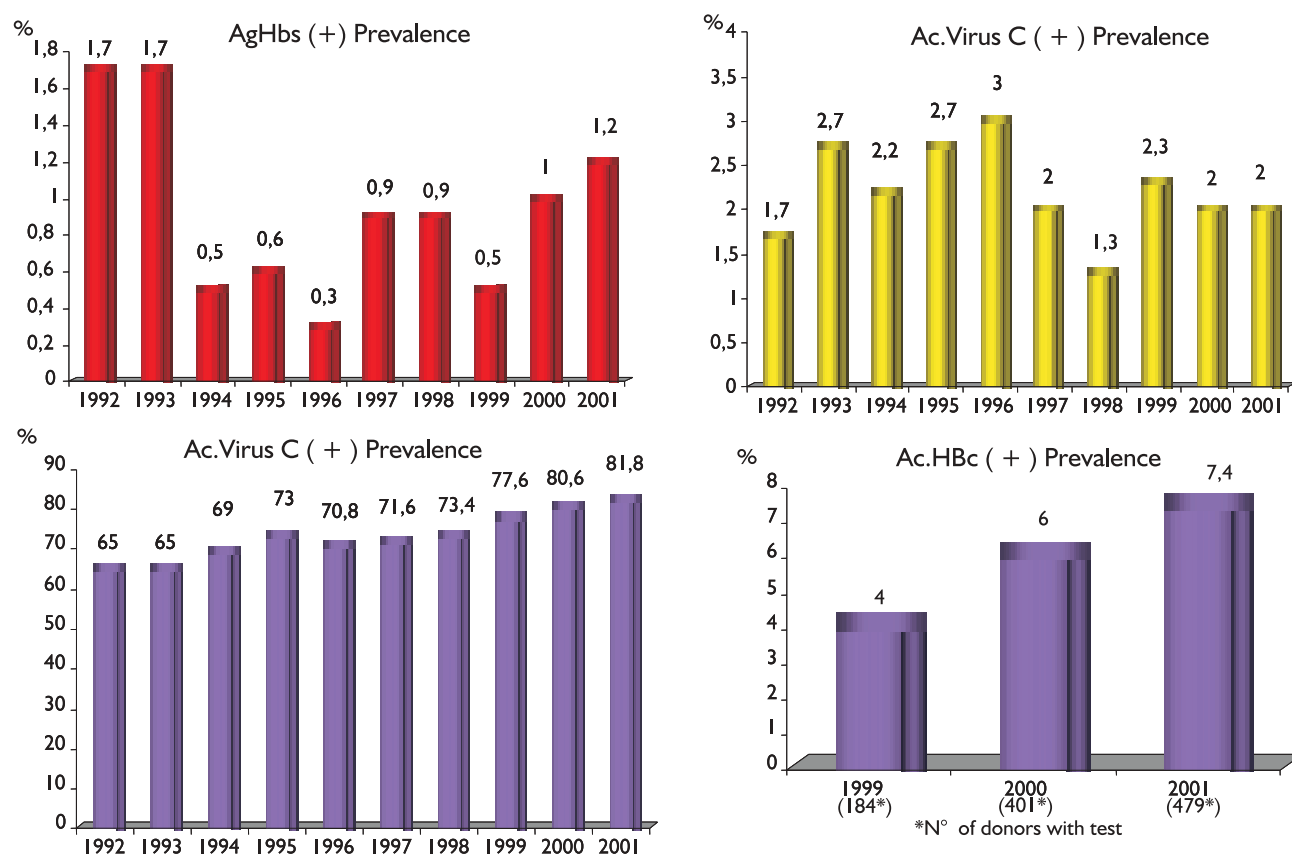


Figure 7. Organ donors Spain 1992-2001.

organs. It is true that organ donation has improved during last years, but it is also true that the number of rejected kidneys has increased as well. Therefore the number of kidney grafts did not rise in parallel with the number of organ donors. Data from the Catalan kidney patient's registry shows that while overall survival is not so different, graft function is much worse with kidneys from donors older than 60, and even worst when those kidneys are grafted in old recipients [11]. Hence, donor age is not the only risk factor, in fact the Eurotransplant program elderly donors for elderly patients, reducing other risk factors such as ischemia time is on the way of recording good results [12]

On the basis of the analysis of the causes for kidney rejection we recorded that only 5% of loses are due to technical problems, and hence with the potentiality to be solved. Most kidneys are discarded due to either, glomerular or vascular sclerosis

It is also true that many organs that some years ago were grafted, ere being discarded nowadays. The current practice of performing kidney biopsies when some risk factor is suspected gives the possibility of either rejecting the organ or performing simultaneous graft of both kidneys into the same recipient This will for sure improve the survival results in forthcoming registry's reports [13] Anyway, at this moment, survival rates and graft function data obtained with older kidneys is far from what would be desirable [13-16], although there are many other donor factors that can be considered as

risk factors for graft evolution:: the extreme ages, bellow 5 years old and over 60 years old, Hypertension or diabetes history, a serologic profile showing viral infection, the cause of death, etc. The challenge is to establish which organs are going to bear higher risks and in which conditions we could utilise them. [13, 15]

We've seen how the age of our donors is increasing progressively, and how more and more kidneys are being rejected every year. We also have seen how the older is the donor the higher is the probability for the kidneys to be rejected. Nearly 60% of all kidneys retrieved from donors over 70 years are rejected. However age is not the only cause for organs to be discarded since 20% of all kidneys from donors between 45 and 59 years are also discarded. This has represented nearly 150 kidneys per year It has also to be outlined that while organ donor's average age is increasing every year, mean age of donors from whom both kidneys are grafted is not so high (42-43 years) and is not increasing. We've included in this group those donors whose kidneys are grafted in the same recipient following a consensus protocol [17] with encouraging results[18]

Percentage of stroke as cause of death is also in correlation with the percentage of organs discarded.: 70 % of donors whose kidneys were discarded died due to stroke. This percentage is reduced to 50% when both kidneys are grafted. Other factors that can affect the organ viability includes pat history of diabetes or

hypertension. Donors whose kidneys were discarded got antecedents of hypertension or diabetes in 50% and 20% respectively. Nevertheless, it can be said that 20% of donors whose kidneys were used had Hypertensive history and 6% got diabetes. This data did not differ from what was previously reported [20]. This means that no donor can be discarded solely because of the past medical history, without a complete and careful examination. Moreover other organs seems not to be so far affected as the kidneys are. Those are recognised risk factors for the long term kidney graft evolution. However this does not mean that those organs should be rejected without a complete and careful evaluation [13, 20]

Moreover, it has been recorded that livers from donors with past history of diabetes or hypertension can be grafted, provided the macroscopic inspection, the perfusion and, if necessary, the microscopic assessment is normal, without an increase in the incidence of primary non function, while more detailed data on the basis of a multivariant analysis is still not available [21]

After the analysis of the donor's and kidney's characteristics we know that we can improve the organ availability by 5% if all the technical problems are overcome. But in the other cases, the evidence of kidney damage determined the organ to be discarded

It becomes clear that the coincidence of more than one donor risk factor deserves less survival probability to the graft, but it also becomes clear that our donor population got the characteristics that we have exposed along the previous pages. Moreover the

recipient's characteristics are also in evolution as a reflect of what is the evolution of the general population profile.

It will be necessary to draw up strategies that could be useful to minimise the effect of the so called risk factors. Probably the secret will be to carefully evaluate the presence of these risk factors and the exact consequences of its use, together with the development of strategies of allocation and recipient's management that could contribute to the improvement of the survival. It will be necessary to discard only what needs to be discarded after the deep evaluation not only of the functional characteristics of the organ but also its morphologic features and hence the possible damage, both on glomeruli and interstitium. We need to find the most appropriate recipient on the basis of all these data. We know that elderly patients present with less immunological response, and less metabolic requirements; we know that the use of some immunosuppressive drugs will represent an additional nephrotoxic risk; we know that with those kidneys the less ischemia time the better is the prognosis; we know that we can use both kidneys into the same recipient etc. Moreover a careful follow up of the recipient becomes mandatory, having in mind all the features of both, organ and recipient.

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