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Living donor renal transplant in Spain: a great opportunity

B. Domínguez-Gil* and J. Pascual**

*National Transplant Organization. **Nephrology Department. Ramón y Cajal Hospital.

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The first successful renal transplant was performed in the year 1954 by the group of Joseph Murray, who later on was awarded with the Nobel Prize in Medicine.[1] This was a kidney transplant from a living donor between identical twins, which solved the main obstacle motivating the failure of previous transplants: the HLA dissimilarity between the donor and the recipient and further graft loss due to acute immune injury. This first renal transplant already highlighted one of the peculiarities in living-donor transplantations: the common genetic relationship between the donor and the recipient, which favors antigenic compatibility.

During the first years of transplantation, donation from living donor was the main organ source. The description of the brain death status and the broad acceptation of its diagnostic criteria led to donation while on brain death status becoming the main organ source in western countries. By contrast, in countries with different cultural, religious, socioeconomic, and even legal frameworks, in which the implementation of donation programs from death donor is rendered extremely complex, donation from a living donor still represents the main organ source.

In recent years, two specific characteristics of living donor kidney transplantation have propitiated a renewed interest in recuperating this organ source for organ transplantation in general, and renal transplant in particular: the outcomes obtained and the scarcity of deceased donors.

Correspondencia: *Julio Pascual*
Servicio de Nefrología
Hospital Ramón y Cajal
Ctra. de Colmenar Viejo, km. 9,100
28034 Madrid
julpascual@gmail.com

GOOD SURVIVAL OUTCOMES

The better results obtained from living donor transplantation as compared with cadaver kidney transplant have led to question whether living donor transplant should be the first option to be offered to a patient with advanced renal disease. According to the data from the *Organ Procurement Transplant Network*, the one-year survival rate of the renal graft is 89% in the case of cadaver kidney transplants *versus* 95.1% for those from a living donor, the differences being even wider with a longer follow-up time, with 5-year survivals of 66.5% *versus* 79.7%, respectively.2 Living donor transplantation also offers better outcomes regarding the patient's survival, with a 5-year survival rate of 82% for recipients of a cadaver kidney graft *versus* 90.2% for those with a living donor graft.[2] The *Collaborative Transplant Study* reports similar figures.[3] When we analyze the data on the first renal transplants performed in Europe during the period 1985-2005, the 20-year graft survival rate with censored death is 65% in the case of renal transplants between HLA-identical twins, 45% for renal transplants from a related donor (when the donor and the recipient share one haplotype), and 34% in the case of cadaver renal transplants. The patient's survival rate is also higher, with a 20-year survival rate of 81%, 81%, and 60%, respectively for the three transplantation kinds.

In the present number of *Nefrología*, Guirado *et al.* confirm these better results in the *Catalonian Renal Patients Registry,* although the adjusted analysis makes them to conclude that these differences are due to the different characteristics of the recipients.[4] In the non-adjusted analysis, the 10-year graft actuarial survival rate is significantly higher with a living donor (60% *versus* 54.3%), these differences vanishing when death is censored as a cause of graft loss. The patient's survival rate seems to be better in the case of patients receiving a living donor transplant, although a further analysis confirms what had been repeatedly suspected, which is that the differences are mainly due to a better initial prognosis of the recipients, especially due to the younger age, a shorter pre-transplantation dialysis time, and lower associated mobility at the time of transplantation. This does not reduce the importance of the differences, it just confirms that early transplantation in relation to dialysis therapy is essential for the patient's survival, which with no doubt is the main goal.

DONATION FROM A LIVING DONOR: THE SOLUTION FOR ORGAN SCARCITY

The second reason explaining this renewed interest in living donor transplantation is organ scarcity for transplantation and the possibility that donation from living donor may become a solution to alleviate, at least partially, this situation. Organ scarcity for transplantation is obvious. In our country, 4,188 patients (93.6 pmp) were on the waiting list for kidney transplant on December 31st of 2006, and only 2,157 renal transplants (48.2 pmp) were performed that year.[5] At a European level, and according to the data gathered by the National Transplant Organization for the European Council, 48,966 patients were on the waiting list by the same date, and only 16,819 kidney transplants were done that year.[5]

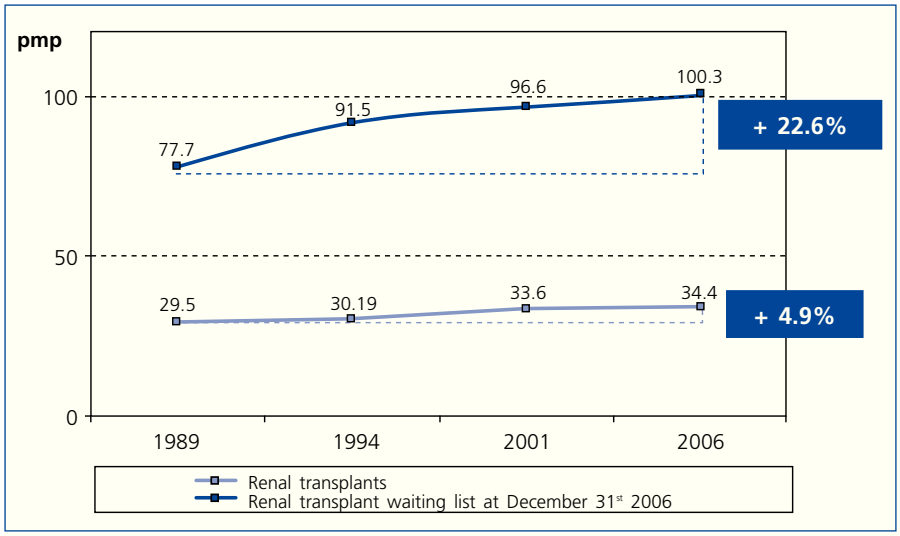


Figure 1. Evolution of the indications for renal transplant (number of patients on the waiting list at December 31st (pmp) *versus* number of renal transplant procedures (pmp) in European countries). The boxes show the percentage increase for renal transplant indications and for renal transplant activity from 1989 to 2006.

On the other hand, the discrepancy between the supply and the demand in renal transplant increases with time and it is expected to keep on increasing. For example, in Europe the indication for renal transplantation (number of patients on the waiting list by the end of the year, pmp) has changed from 77.7 in 1989 to 100.3 pmp in the year 2006. However, the renal transplant activity has little changed from 29.5 to 34.4 procedures done pmp (fig. 1). This implies that during a 17-year period, in Europe the indication for renal transplantation has increased by 22.6%, whereas the activity has only increased by 4.9%. Thus, today's dramatic scarcity will worsen in the future.

In spite of the intensive activity in organ and tissues collection from deceased patients carried out in Spain, this activity still is insufficient to keep up with the demands in our population. The calculations done to estimate the potential number of brain dead donors yield a maximum reachable number of 45-50 donors pmp.[6] According to the cumulated data from the Quality Assurance Program in the Donation Process in the period 1999-2004, we know that 51.3% of deceased patients in a brain death status at the ICU become true donors and that 27.6% of brain dead patients at the ICU do not become donors because of medical contraindications to donation.[7] According to these data and knowing that in the year 2006 the number of absolute donors in Spain reached the number of 1,509, our donation potential (brain deaths at the ICU without medical contraindication) may be estimated at 47.7 donors pmp for that year.

We are still far from reaching that potential, but even in the case of reaching it and that the kidney discard rate in our country would be 0%, we would not be able to solve the historical or the future needs in renal transplantation. Donation in asystolia is another organ source for transplantation. However, the activity is rendered limited without the use of donors within the category of Maastricht type III, which does not seem to be an acceptable reality in our country at the present time due to ethical and legal issues. Thus, independently of the better results obtained from living donor renal transplant, this type of transplants has become a real need in Spain in order to increase the transplantation possibilities for our population on the waiting list, especially for the young population, as we will see next.

The decrease in mortality related with head trauma as a result of the fortunate decrease in motor vehicle accidents, has led to a descent in the number of young donors pmp. The activity has been maintained at the expense of an evolution in the donor's profile, deceased mainly because of intracranial hemorrhagic pathology[8,9] (fig. 2). Thus, the donors' age increases so that in the year 2006 almost 40% of deceased donors were older than 60 years[8,9] (fig. 3). The need for matching the renal mass -and thus the age- between the donor and the recipient, together with the paucity of young donors, makes that the likelihood of renal transplantation among young patients is particularly decreased. Precisely, young dialysis patients, or even pre-dialysis ones, as suggested by Guirado *et al.*,[4] are those with the greatest need of this classical, and currently an alternative, source of organs for transplantation.

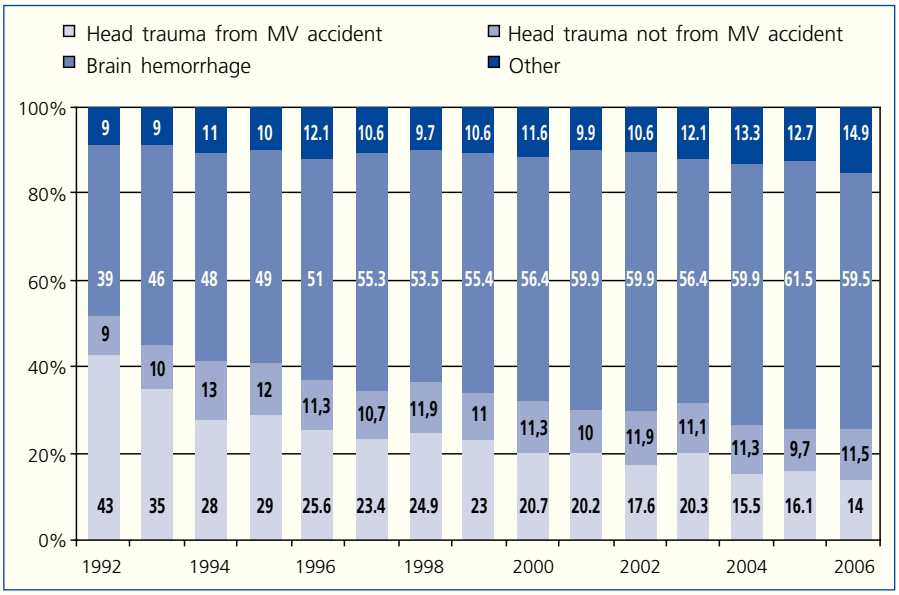
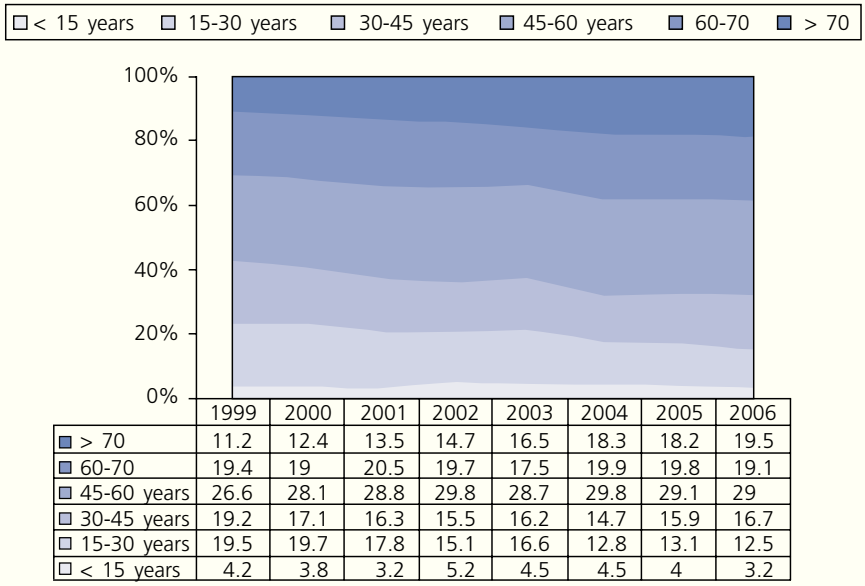


Figure 2. Evolution in the cause of death among organ donors in Spain[8,9].



	1999	2000	2001	2002	2003	2004	2005	2006
> 70	11.2	12.4	13.5	14.7	16.5	18.3	18.2	19.5
60-70	19.4	19	20.5	19.7	17.5	19.9	19.8	19.1
45-60 years	26.6	28.1	28.8	29.8	28.7	29.8	29.1	29
30-45 years	19.2	17.1	16.3	15.5	16.2	14.7	15.9	16.7
15-30 years	19.5	19.7	17.8	15.1	16.6	12.8	13.1	12.5
< 15 years	4.2	3.8	3.2	5.2	4.5	4.5	4	3.2

Figure 3. Evolution of organ donors' age in Spain[8,9].

LIVING DONOR TRANSPLANTATION IN SPAIN

Based on the argumentation exposed, the global attitude of the system towards performing living donor transplants has been modified through time. This attitude change has permeated the discourse derived from the recommendations issued by expert groups, such as the Transplant Commission of the European Council. In the year 2007, this organization stated that living donor transplant ought to be a "restrained activity". By contrast, in the year 2002, this same institution recommended that living donation "may be performed to benefit a recipient with a close personal relationship with the donor, which is defined by law, or in the absence of this relationship only under those circumstances defined by the law and with the approval of an appropriate independent body".[10]

This therapeutic option has gained interest in our country as shown by the slow but progressive increase in the living donor transplantation activity in the last years (fig. 4). In this way, in the 1990s living donor transplantation accounted for 1%-1.5% of the whole renal transplantation activity in Spain; in the last year, this percentage has increased to 4.7%.[8] This activity is very much lower than that observed in neighbor countries (fig. 5). In fact, in the year 2006, 2.3 pmp living donor transplants were performed in Spain, while some European countries have figures of 15 procedures pmp, and 21.4 pmp in the USA.[5]

Finally, it may be expected that the living donor transplantation activity will keep on increasing in Spain. In fact, 23 centers were performing this type of transplants in the year 2007, and three other centers are expected to start with this activity within the near future (fig. 6).

BARRIERS TO LIVING DONOR TRANSPLANTATION IN SPAIN

There are mainly two barriers precluding a rapid increase in the living donor transplantation activity in Spain: 1) the absence of an indication from the professionals taking care of patients with advanced renal failure; and 2) the lack of experience in many of our transplantation units. Living donor transplant is not offered as another therapeutic option. According to one survey performed just three years ago among dialysis patients, 59% of them had not receive information on this kind of transplant, and 83.4% stated that their doctor had not tell them about this therapeutic option.[11] The main reason for not offering this option seemed to be, according to what interviewed nephrologists expressed, the fact of considering that the renal transplant activity from deceased donor was sufficient in Spain. We have no data on whether or not the frequency of offering living donor transplantation varies according to the characteristics of the center where the patient is followed-up or dialyzed. However, we may reason that this situation occurs more frequently in those centers without transplantation activity.

Another possible barrier to not offering this option is the lack of knowledge about how this issue should be exposed to the relatives, either actively or only if the patient or his/her relatives ask for it.

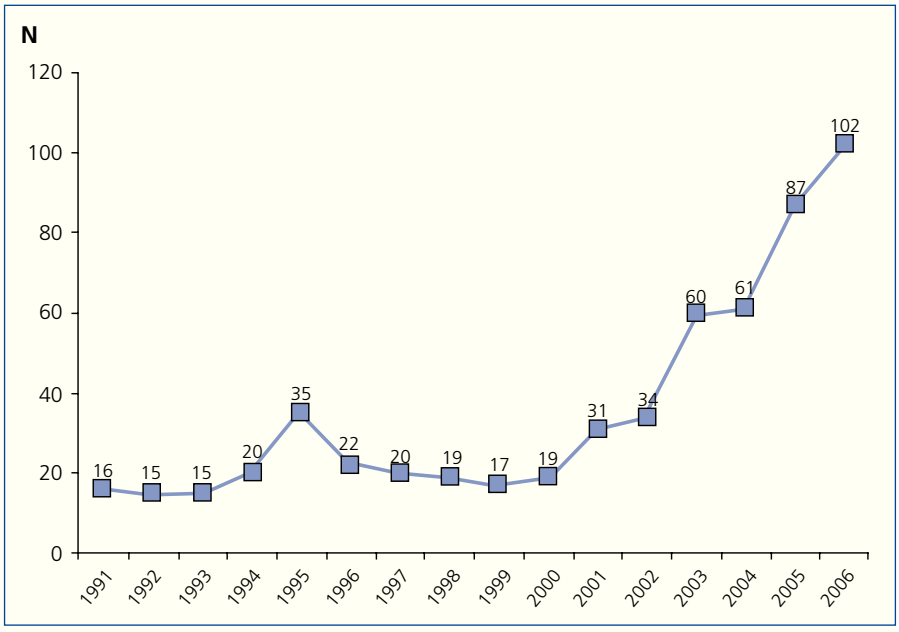


Figure 4. Evolution in the number of living donor transplants in Spain[8].

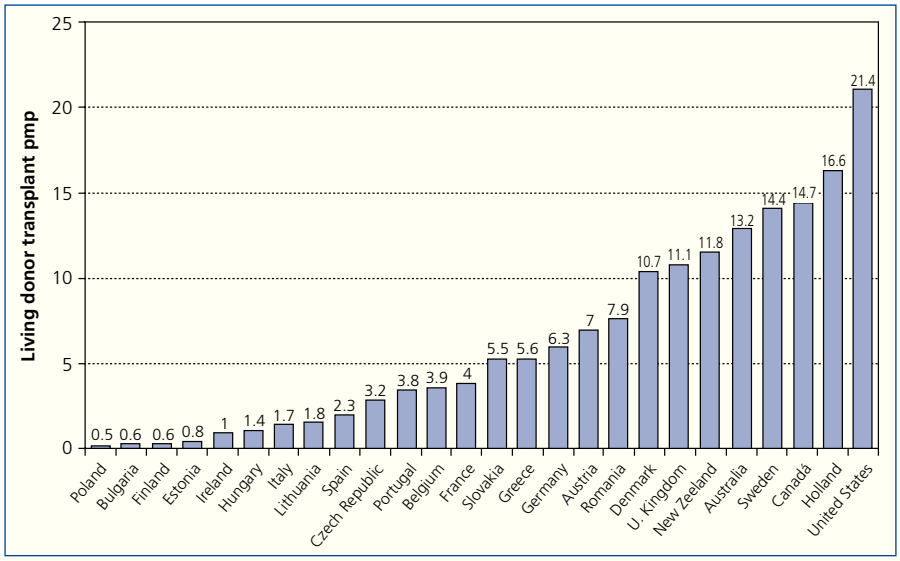


Figure 5. Living donor transplants (pmp) performed in different European countries, Australia, Canada, USA, and New Zeeland, in the year 2006[6].

In a recently published study describing the psychological barriers to living donation, the main reason exposed by the patients on the waiting list not seeking this option was their refusal to discuss the issue with their potential donors.[12] Among the patients on the waiting list that were candidates for living donor transplant but that had no actively seek that option, many interpreted as a negative answer to donation the lack of an spontaneous offer from their potential donors. However, this interpretation was not always correct: more than one third of the potential donors were prone to be considered as such. Also many patients feared to ask their relatives and close friends because they were afraid of receiving a negative answer. The patients on a waiting list that were not in favor of living donor donation gave as the main reason the fear to nephrectomy in the donor. This article highlights the non-strictly medical difficulties when offering this therapeutic option, before which the treating physician may feel somewhat disoriented. In addition to the need for specific education on this issue, the other possible solution is the creation at the hospital setting of personnel that would be in charge of informing, posing this option, and orienting the patients and their relatives, following the indications set up by the professionals in charge of the clinical follow-up.

In conclusion, not offering this option to the patients or even not posing it to the patients or their relatives reflects, more or less apparently, the fear to nephrectomy in a healthy person, which from the health care's viewpoint it infringes the first rule in Medicine, "*primun non nocere*". The international consensus document of the Amsterdam Forum describes how to approach, assess, manage, and do the clinical follow-up in the case of living kidney donors.[13] With no doubt we should pursue its universal implementation in spite of the eventual occurrence of complications in the short, intermediate, and long terms. The literature shows a mortality rate from living kidney donation of 0.03%.[14] The mortality within the immediate post-surgical period is also low, although it varies depending on the surgical approach used to perform the nephrectomy.[14]

The long-term follow-up of living kidney donors has not generally shown the presence of more medical complications than those described in the general population. However, losses to follow-up and the comparison with the general population may not be appropriate given that living kidney donors have better health status, observations that have clearly been reported in a review article called "*absence of proof is not proof of absence*".[15] In fact, promoting living donor transplantation necessarily implies the obligation of detailed collection of all the complications developed by the living donor in the short, intermediate, and long terms, including medical, psychological, and social complications. Only by increasing the evidence on the evolution of the liv-

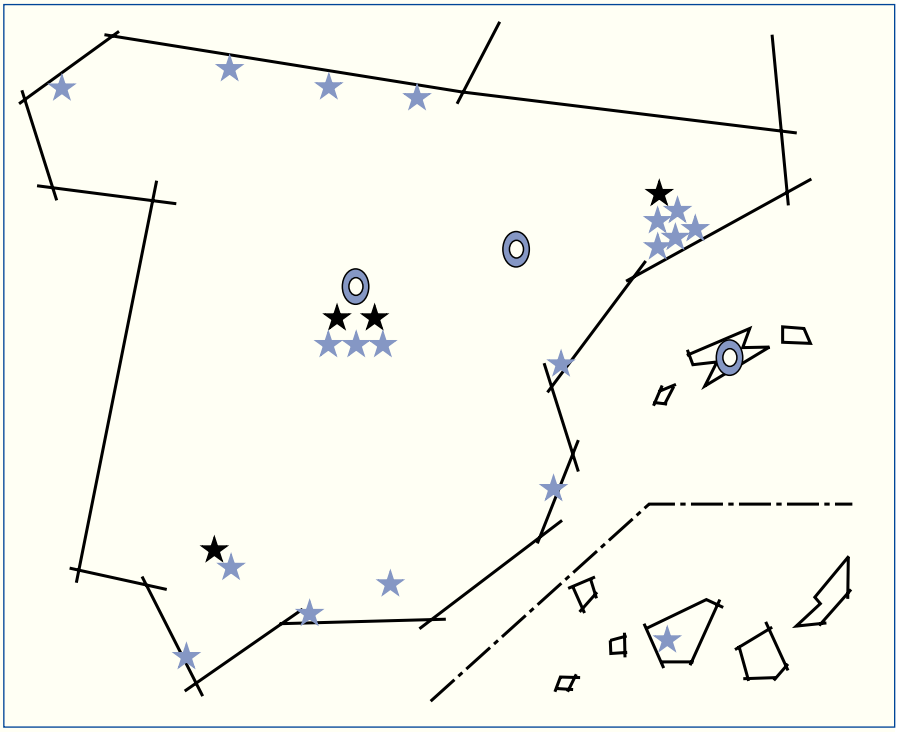


Figure 5. Spanish centers with living donor transplant activity. Year 2007. (Red stars: centers for adult patients; black stars: pediatric centers; blue circles: centers pending to start this kind of activity).

ing kidney donor we will be convinced of the relative harmfulness of nephrectomy in the donor, get more precise in the circumstances precluding this option, and provide complete information to potential living donors.

The second barrier to the increase in this activity is the lack of experience in donation and transplantation from a living donor by many of our transplantation teams. It is essential to promote the education of our teams by facilitating the progressive introduction of new instrumental procedures making donor's nephrectomy easier, mainly through laparoscopic nephrectomy. Although we should promote the development of this type of techniques, they should not become a *sine qua non* condition for the setting-up of a living donor program, but an added value. The practice of the classical open nephrectomy should not be "demonized" provided that this technique may represent the most appropriate one in a particular setting.

CONCLUSION

Living donor transplantation definitely offers clear advantages as compared to dead donor renal transplant. On the one hand, these advantages are individual, since they benefit the patient regarding his/her living expectancy. But even more, as Guirado *et al.* point out in their article, living donor transplant offers collective advantages: it helps solving the issue of organ scarcity, which will increase with time and that mainly threatens our young population. Just by increasing the living donor transplant activity from 5% to 15% we would be performing about 300 living donor transplants per year, which represents a great opportunity to increase our patients' probability of receiving a transplant.

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