Donation and Kidney Transplantation Rates

Since it was first performed in 1965, the evolution of kidney transplantation (KT) in Spain has been determined by that of deceased donation. In 1989, a specific coordination model was implemented in Spain, which already counted on a Transplantation Law, had the technical capacity for the practice of KT, and a public national health care system (NHS) with universal coverage of the population. The so-called Spanish Model on Organ Donation and Transplantation helped the country evolve from 14 donors per million population (pmp) in 1991 to 49 donors pmp in 2019 (2): (1) a broad implementation of the practice named intensive care to facilitate organ donation, defined as the initiation or continuation of intensive care measures in patients with devastating brain injury in whom curative treatment has been deemed futile, to incorporate organ donation into their end-of-life care plans (3); (2) the successful use of organs from aged and very aged donors following an old-for-old allocation strategy (4); and (3) the expansion of donation after the circulatory determination of death (DCDD), which has exponentially increased in the last decade, so it now represents nearly 30% of the overall deceased donation activity (5). As a result, KT progressively increased to 3423 procedures (72.8 pmp) in 2019 (Figure 1). There are currently 35,183 patients (748 pmp) living with a functioning graft, 55% of prevalent patients with ESKD (6).

Most KT are obtained from deceased donors (Figure 1). Of note, DCDD currently contributes to 29% of the KT activity. In particular, 27% of KT derive from controlled DCDD donors (who died after the decision to withdraw life-sustaining therapies that were no longer deemed beneficial), whereas 2% derive from uncontrolled DCDD donors (who died after an unsuccessfully resuscitated cardiac arrest). Most potential and actual controlled DCDD donors are people who die (after the decision to withdraw life-sustaining therapies) as a result of a devastating brain injury who did not meet brain death criteria. Approximately 5% of controlled DCDD donors die as a result of terminal heart, lung, and neurodegenerative diseases. The contribution of live donation progressively increased from the beginning of this century, reaching a peak in 2014, then decreased again as deceased donation expanded. At present, 10% of KT derive from live organ donors. The increase of live KT obeys to a changing attitude of professionals and authorities toward the consideration that it must be systematically offered as a treatment option to patients with advanced kidney disease, ideally in a preemptive fashion. Its expansion has been channeled through issuing guidance and standards of practice (7), the removal of technical barriers (through blood group ABO- and HLA-incompatible KT programs and the Spanish national kidney paired exchange scheme) (8), the training of professionals, and the implementation of measures targeted to ensure the overall protection of the live organ donors.

The age of deceased kidney donors is worth mentioning. At present, 28% are aged ≥70 years. Dual transplantation is a practice exceptionally performed in Spain. Organs from aged donors are allocated following an old-for-old strategy. Indeed, using organs from donors aged ≥60 years has allowed for an expansion of the age of patients on the waiting list (WL). The profile of kidney donors reflects the capacity of the system to adapt to that of potential organ donors in Spain, where mortality relevant to organ donation is low, and there is a fortunate reduced number of deaths from non-natural causes.

The Waiting List for Kidney Transplantation

The number of patients ever active on the kidney WL has progressively increased over the years, likely as a result of more flexible listing criteria. Indeed, age of KT recipients has increased along time, with almost 20% aged ≥70 years and with a greater burden of comorbidity. At the end of 2019, 3933 of the 29,109 (14%) patients under renal replacement therapy with dialysis were active on the kidney WL.

There is a national program in place to prioritize patients with a calculated panel reactive antibody or cPRA ≥98% on the WL on the basis of single-antigen bead tests since 2015. Kidneys from donors who meet agreed criteria are allocated to patients who are highly

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sensitized first, if a virtual crossmatch is negative. These patients represented 12% of those on the WL in 2019.

Costs of Hospitalization after Kidney Transplantation
Hospitalization episodes are grouped according to the all patient refined–related diagnostic groups (RDG) classification in the Spanish Registry of Hospital Discharges (Registry of Specialized Care Activity Basic Minimum Data Set). The average length of hospital stay for the RDG KT is 16.1 days, and 14.3 days for adjusted mean stay (excluding extreme stays) with a cost ranging from €17,702 to €47,565, according to severity level (9). Several cost analyses of KT carried out in Spain in recent years show it is highly cost effective compared with dialysis (10).

The length of hospital stay is longer than in the United States, where the mean length is 5.5 days (11). The characteristics of the Spanish public health system, the greater acceptance of older and comorbid recipients, and the increasing proportion of expanded criteria donors with a very small number of live donors may explain these differences. The early hospital readmission rate, a well-accepted metric of hospital quality, must also be considered. In a study carried out in the Autonomous Community of Madrid, these early readmissions after a hospital discharge after KT were almost half than in the United States (15% versus 30%) (11,12).

Professionals Who Typically Perform Kidney Transplants and Provide Post-Transplant Care
Urologists have been responsible for KT surgery in Spain since the first procedures were performed in 1965. Urology is the only surgical specialty that includes KT as a mandatory training program for residents (13). Exceptionally, in some programs, other surgeons, especially vascular surgeons, participate in transplant surgery with urologists. In Spain, nephrologists are responsible for the care of KT recipients in the short and long term. Until recently, this task was exclusively performed by the transplant nephrologist. The high KT rates have determined an exponential increase in the number of recipients with a functioning graft. For this reason, although some centers continue to carry out long-term follow-up of all recipients, many

Table 1. Basic elements of the Spanish model on organ donation and transplantation

| Elements | 
|----------|
| 1. Adequate legislation and technical capacity |
| 2. Donor coordination network, structured at three inter-related levels: national, regional, and hospital |
| 3. Specific features of donor coordination teams: |
| • Located in the hospital |
| • Lead by physicians, mostly intensive care specialists |
| • Part-time dedication |
| • Designated by the direction of the hospital |
| 4. Central office as a technical agency that continuously supports the development of the deceased-donation process |
| 5. Quality Assurance Program of the deceased-donation process to continuously assess the potential of donation and evaluate areas for improvement (on the basis of internal and external audits) |
| 6. Hospital reimbursement |
| 7. Great effort in professional training covered with governmental funds |
| 8. Special relationship with the mass media |

Figure 1. | Evolution of kidney transplant activity in Spain by donor type. The activity is represented in absolute numbers and rate of kidney transplants per million population. DCDD, donation after the circulatory determination of death; DND, donation after the neurologic determination of death; pmp, per million population; Tx, transplant. Source: Organización Nacional de Trasplantes.
transplant hospitals have promoted the coordinated follow-up with the nephrology departments of nontransplant centers. Guidelines have been developed to ensure good coordination with regular interaction between the transplant center and the community nephrologist (14). Usually, care for all recipients is provided during the first 6–12 months after KT by the transplant nephrologist and, subsequently, recipients with stabilized KT continue their follow-up by the nephrologist of the nontransplant hospitals or alternate between transplant and nontransplant centers.

In contrast, the primary care physician collaborates with the nephrologist, especially in vaccination programs, nonserious health problems, and the control of cardiovascular risk factors.

Coverage of Transplant Surgery and Immunosuppression Costs
Population covered by the NHS include all Spanish nationals and foreign citizens authorized to reside in Spain. The coverage comprises, among other things, care activities for prevention, diagnosis, treatment, and rehabilitation carried out in health care centers (15). Outpatient pharmaceutical services are subject to copayment on the basis of three criteria: income, age, and extent of disease (user payment from 0% to 50%). Some drugs for chronic diseases, such as immunosuppressants, have a reduced contribution for all users who pay only 10% of the price with a maximum of €4.24 per container. For patients who are hospitalized, the pharmaceutical prescription is fully covered by the NHS.

Health care costs are covered by public funding obtained from taxes and, to a lesser extent, by agreements between the NHS and private insurance providers. Transplant surgery, immunosuppressants, and other health services required by patients who have undergone KT throughout their life are covered by the NHS under the conditions described above. Very exceptionally, a nonresident foreign citizen could undergo a live donor KT (never from a deceased donor), covered by their insurance or with direct payment, with prior approval from the NHS.

Graft and Patient Survival 1, 5, and 10 Years after Transplant
The information on the outcomes of KT in Spain derives from the Spanish Registry of Renal Patients (Registro Español de Enfermos Renales). This results from the sum of renal registries of the 17 Autonomous Communities and the two Autonomous Cities that conform Spain, which decide the information collected and shared, posing difficulties to build global information. An analysis of 20,363 KT performed during 1975–2012 revealed that death-censored graft-survival was 90%, 82%, and 70% at 1, 5, and 10 years after transplantation. Most were first transplants (90%) (16).

The two most active regional registries in the country offer more recent data on survival. Of 11,937 KT from deceased donors performed in 1984–2018, the Registry of Cataluña (Registre de Malalts Renals de Catalunya) reported a patient and death-censored graft-survival of 95%, 86%, and 72%, and of 90%, 79%, and 65%, at 1, 5, and 10 years, respectively (17). Similarly, of 7423 KT performed during 2000–2018, the Registry of Andalucía (Sistema de Información de la Coordinación Autonómica de Trasplantes de Andalucía) described that patient and death-censored graft survival were 96%, 89%, and 79%, and 94%, 88%, and 78% at 1, 5, and 10 years (18). The Registry of Cataluña shows progressive significant improvement in 5-year death-censored graft-survival until the early 2000s, but not thereafter (65% for the period 1984–1989, 75% for 1990–1995, 80% for 1996–2001, 83% for 2002–2007, and 83% for 2008–2018). This is likely explained by the changing profile of both deceased donors and recipients, of increased aged, and a greater burden of comorbidity. A comparative analysis of Spain versus US transplant outcomes published in 2012 showed better patient survival for Spain and similar death-censored graft survival (19).

For living-donor KT outcomes, of 1996 transplants performed in 1984–2018 in Cataluña, the Registry of Cataluña reported a recipient and death-censored graft-survival of 99%, 96%, and 90%, and 97%, 90%, and 79%, at 1, 5, and 10 years. Of 591 living-donor transplants performed in 2000–2018, Registry of Andalucía reported patient survival of 99.9%, 99%, and 94%, and death-censored graft survival of 97%, 95%, and 87% at 1, 5, and 10 years.

The Major Barriers to Successful Kidney Transplantation
The progressive increase in donation and transplantation rates in Spain since 1989 has expanded KT opportunities for patients with ESKD. Nevertheless, there are still challenges—probably shared with other Western countries—that can be grouped as follows:

1. Unequal access to transplantation: inequity in the access to the kidney WL still exists. This issue needs to be thoroughly addressed by the nephrology community, with clear information to both professionals and patients regarding the limited number of absolute contraindications for KT. Besides, different donation rates (i.e., the highest rate is 89.7 donors ppm in one region and the lowest 34.2 ppm) and policy to accept kidneys for transplantation result in inequity too.

2. Insufficient number of kidneys available for transplantation and suboptimal quality: although the number of deceased donors in Spain is very high compared with other countries, the availability is still inferior to the transplantation needs. This is particularly the case in young patients, because the expansion of deceased donor KT has greatly relied on aged and very aged individuals (4). Besides, the quality of kidney grafts influences the half-life of the graft and the need of relisting for KT if graft failure. It is hence imperative to further promote live KT, still insufficiently developed in Spain. Moreover, efforts must be made to better understand the limits in the utilization of expanded criteria donor kidneys for transplantation.

3. Need to engage the more active participation of the mature renal transplant patient in their own health care regarding both the control of cardiovascular and other risk factors and compliance with the immunosuppressive treatment: the change from a paternalist health care
system to a system in which coresponsibility applies will probably affect the results of transplantation too. The incorporation of patient-reported outcomes to existing and evolving registries must also be considered in this approach.

Disclosures
M. Crespo reports receiving speaker’s honoraria from Astellas, Chiesi, Hansa, and Novartis; reports being Coordinator of the Transplant Group of the Spanish Society of Nephrology, and member of the the Board of the Descartes Group - the Transplant working group of the European Renal Association. A. Mazuecos reports receiving speaker’s honoraria from Astellas, Chiesi, Novartis and GSK; reports being member Coordinator of the Transplant Group of the Spanish Society of Nephrology and councilor on the Board of the Spanish Society of Nephrology. All remaining authors have nothing to disclose.

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Author Contributions
M. Crespo was responsible for the methodology; M. Crespo, A. Mazuecos and B. Dominguez provided supervision; and all authors conceptualized the study, wrote the original draft, and reviewed and edited the manuscript.

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