Global Perspective on Kidney Transplantation: France

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Gillian Divard and Valentin Goutaudier

Key Points:
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Abstract:

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Global Perspective on Kidney Transplantation: France

Gillian Divard†,1 and Valentin Goutaudier1

1Université de Paris, INSERM, PARCC, Paris Translational Research Centre for Organ Transplantation, Paris, France

†Corresponding author:
Dr Gillian Divard
Paris Translational Research Centre for Organ Transplantation
PARCC-INSERM U970
56 rue de Leblanc, 75015, Paris, France
Phone: +(33)-6-31-42-16-63
Email: gillian.divard@inserm.fr
INTRODUCTION

France is a country in western Europe, with a population of 67.06 million in 2020\(^1\). This country has a universal health care system, financed by a compulsory health insurance taxation based on workers income which refunds patients 70\% of most health care costs and 100\% for costly or long-term diseases, such as chronic kidney disease. Chronic kidney disease affects nearly 3 million people, and the prevalence increase by 2\% each year\(^1\). Among them, 89,692 are treated by dialysis or received a kidney transplant. France has been a pioneer in transplantation with the first kidney transplant performed in 1952\(^2\). After two decades of transplants with living donors, the first bioethics laws were enacted in 1976, authorizing deceased donor procurement and instituting three rules for organ donation: 1) all adult residents are presumed to be consenting to donate except in case of expression of refusal during lifetime 2) donation is anonymized and 3) donation is free of charge. Since 2004, organ procurement is organized by the Biomedicine Agency, which is in charge of ensuring equity and safety of organ allocation, and collecting donor characteristics, recipient characteristics and follow-up through the French national database called CRISTAL. The national allocation system for deceased donor is based on a scoring system from a local level and a national level and also some national allocation priorities (Figure 1). Kidney transplantation is currently performed in 47 centers mostly public university hospitals, of whom 14 perform 60\% of the transplants\(^3\).

NUMBER OF KIDNEY TRANSPLANT RECIPIENTS

Since the start of the French national registry in 1959, a total of 91,565 kidney have been transplanted. Among them, 42,409 are still functional and correspond to a prevalence of 628 per million people in the general population\(^3\), while 50,501 patients are on dialysis. In 2019, 3,643 kidney transplants were performed, representing a ratio of 53.9 per million
people and placing France in second place in Europe behind Spain\(^3\). Kidney transplantation activity, while increasing continuously, is far to cover the rising demand, and inexorably patients accumulate on the waiting list\(^4\) (Supplementary table S1). To tackle this challenging obstacle, France have made considerable efforts for promoting transplant from living donors, and the organ procurement of donors after cardiac arrest was reintroduced in 2006\(^4\). In 2014, a significant milestone was also reached with the opening of a program authorizing to recover kidneys from Maastricht III non-heart beating donors, allowing to perform 826 new transplants in five years with similar or even better early outcomes than brain dead donors\(^3,5,6\).

**NUMBER OF KIDNEY TRANSPLANT CANDIDATES ON THE WAITLIST**

The growth rate of the number of people on the waiting list increases from year to year (further details are provided in the Supplementary table S1), with 16,181 patients waiting for a transplant on January 1, 2020, including 5,269 new patients on the waiting list, compared to 4,557 new patients in 2013 (+ 15.6%). Among these candidates, 8,642 are active and 7,539 are inactive (temporary contraindication) on the list\(^3\). The median waiting time between registration and transplantation increased progressively in recent years and has reached 22.6 months\(^3\). It is important to note that there are discrepancies according to age categories and regional registration areas, reflecting various appreciations in indications for kidney transplantation\(^7\). In order to mitigate these discrepancies, the Biomedicine Agency modified its allocation system score in 2015, by improving the quality of age pairing and integrating road distances in minutes between the sampling and transplant locations for assigning the graft.

**PERCENT OF LIVE DONOR VERSUS DECEASED DONOR TRANSPLANTS**
In 2019, 510 kidney allotransplantations from a living donor were performed, representing 14% of the total number of kidney transplants. This ratio remains insufficient, so two main efforts were made for increasing this activity. First, French bioethics laws were revised in 2011, for allowing people with a close and emotional bond for at least two years with the recipient to donate a kidney. Secondly, a paired kidney exchange program was introduced in the event of blood group incompatibility between the donor and the recipient. However, this program is struggling to develop since it requires complex logistic, and some centers also perform ABO incompatible transplants. Consequently, it allowed only 12 kidneys transplants since its setting up in 2013. Facing the predictable increase in the number of candidates, all efforts should be put together for increasing the number of living donor transplants, and this activity is largely promoted by the Biomedicine Agency. Concerning deceased donors, 89% were brain dead, 1% were Maastricht II non-heart beating and 10% were Maastricht III non-heart beating donors in 2019. Furthermore, among the donors after brain death, 52% were expanded criteria donors. Further details on the evolution of organ procurement according to the donor type during the last 10 years are provided in the Supplementary table S2.

LENGTH OF HOSPITAL STAY AFTER KIDNEY TRANSPLANTATION

The median length of hospital stay after kidney transplantation is 14 days IQR [11-19]. It mainly depends on hospital logistics, medical resources, donor type, and recipients’ characteristics. Moreover, the absence of ambulatory facilities like outpatient clinics or day-hospitalization significantly increases length of stay. To note, some patients, especially elderly or frail, can be hospitalized much longer with a median of 16 days IQR [12-22] after 65 years old. Hence, some centers are organizing close care networks with rehabilitation
centers for reinforcing the postoperative period and improving morbi-mortality and quality of life after such transplant.

**SURGEONS WHO PERFORM THE KIDNEY TRANSPLANTS**

Since 1952, kidney transplants are historically performed by urologists in France\(^2\). Kidney procurements and low surgical risk transplants from deceased donor are mainly performed by junior urologists. High surgical risk transplants and living donor transplants are usually performed by senior urologists, accompanied by a junior. In case of high-risk vascular transplant, such as a transplantation on vascular prothesis, the surgery can also be performed with the help of a vascular surgeon. To note, kidney transplant surgery is rarely an exclusive activity for surgeons. This may increase cold ischemia time, however the mean cold ischemia time was 15.4 hours in 2019 and tend to decrease in the past 10 years\(^3\).

**TRANSPLANT SURGERY COSTS**

France is based on a national solidarity system and takes in charge a list of serious and/or chronic diseases requiring a prolonged and costly treatment. Chronic kidney failure is one of them and is fully covered for the care related to this pathology. The effective surgery costs from the removal to the transplantation is estimated of 13,835.44 € (16,340.90$) for a deceased donor and 13,601.66 € (16,064.78$) of the donor for a living donation (including the follow-up)\(^9\). However, these amounts could significantly increase according to the patient's postoperative complications and comorbidities. These costs are integrally covered without out-of-pocket expenses and advance payment for the patient.

**POST-TRANSPLANT CARE FOR KIDNEY TRANSPLANT RECIPIENTS**
Historically, post-transplant care is usually provided by transplant nephrologist. The recipient is hospitalized in a nephrology/kidney transplant department before and right after the transplant surgery. Then, the follow-up is carried out either in the transplant center or with the nephrologist who followed the patient before the transplant, or jointly. Some guidelines of good practices were published for the management of a kidney transplant recipient by the French High Authority for Health in 2007. The initial follow-up is weekly during the first 3 months then bi-monthly until 6 months and monthly until 1 year. After 1 year, the follow-up is variable depending on the centers and the patient's condition every 1 to 4 months, according to the centers and the patients’ conditions.

**COSTS OF IMMUNOSUPPRESSION**

The cost of immunosuppression and other medications related to the transplant are covered by national insurance. However, patients have little out-of-pocket expenses with a fixed price per box of medication up to a limit of 50 € (59 $) per year for medical expenses related to their pathology.

**GRAFT AND PATIENT SURVIVAL AFTER TRANSPLANT**

The short term allograft survival has steadily improved in France, with a current survival rate of 91.9% at 1 year. However, long-term survival has quietly decreased over the last twenty years, with a current allograft survival rate of 78.1% at 5 years and 59.5% at 10 years (supplementary figure S1). The same thing is observed regarding patient survival, with a current survival rate of 96.5% at 1 year, 87.8% at 5 years and 74.6% at 10 years. The main hypothesis for this relative decrease is that the age of donors and recipients have increased, as well as the complexity of recipients with more comorbidities and a growing immunological risk.
MAJOR BARRIER TO SUCCESSFUL KIDNEY TRANSPLANTATION

The major barrier to successful kidney transplantation in France is the constant increase in the immunological risk of patients. Many barriers have been crossed with the desensitization protocols and the multiple transplantations, but antibody-mediated rejection remains the main cause of allograft failure in kidney transplant\textsuperscript{11}. For this purpose, national priorities have been created for hypersensitized patients (\textit{ie}, with a virtual calculated panel reactive antibody greater or equal to 85\% or 70\% at time of transplant). These programs represent 13.3\% of transplants performed in 2919 (Table 1). The main program since 2005 is the Authorized antigens program, similar to the Acceptable mismatch program from Eurotransplant. To be included in this program, patients must have a cPRA greater or equal to 85\% and a serum tested with Single Antigen Flow Beads assays every 3 months to detect potential anti-HLA antibodies emergence and then prevent unexpected positive crossmatches. This program initially causes several problems by authorizing the transfer of young donor grafts to immunized elderly recipients, a rule with an age criterion was added later to solve this problem. Another problem was the exponential increase of patients in this program with the advent of high-definition techniques to detect anti-HLA antibodies especially for class II anti-HLA antibodies and the heterogeneity of practices across HLA laboratories to classify antigens as prohibited. The Biomedicine Agency is working to homogenize practices across HLA laboratories.
Disclosures
The authors have nothing to disclose.

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Supplemental Materials
Table S1. Evolution of the number of kidney transplants and the number of candidates on waiting (active and inactive) list during the last 10 years.
Table S2. Evolution of organ procurement according to the donor type in France during the last 10 years.
Supplementary Figure S1: Graft survival according to transplant period
References
Table 1. Type of allocation of kidney transplants from donors after brain death in 2019

<table>
<thead>
<tr>
<th>Type of allocation</th>
<th>Number of transplants (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local or regional based on the scoring system*</td>
<td>1384 (49.7%)</td>
</tr>
<tr>
<td>National based on the scoring system*</td>
<td>788 (28.3%)</td>
</tr>
<tr>
<td>Dual kidney transplant</td>
<td>19 (0.7%)</td>
</tr>
<tr>
<td>Priorities:</td>
<td>592 (21.3%)</td>
</tr>
<tr>
<td>Urgent</td>
<td>11 (0.4%)</td>
</tr>
<tr>
<td>Highly sensitized patients</td>
<td>371 (13.3%)</td>
</tr>
<tr>
<td>Sensitized patients</td>
<td>30 (1.1%)</td>
</tr>
<tr>
<td>Combined transplant</td>
<td>115 (4.1%)</td>
</tr>
<tr>
<td>Children</td>
<td>64 (2.3%)</td>
</tr>
</tbody>
</table>

*French scoring system takes into account dialysis duration, time on the waiting list, recipient age, donor recipient HLA and age matching, recipient’s matched donor potential and travel time between procurement and transplant centers.

Adapted from the [Rules of allocation of organs from deceased donor], Agence de la biomedicine, 2015.