ORIGINAL ARTICLE

Transplant center characteristics associated with living-donor kidney transplantation: a cohort study with a hierarchical modeling approach

Valérie Châtelet[1], Philippe Gatault[2], Marc Hazzan[3], Dany Anglicheau[4], Guy Launoy[5], Thierry Lobbedez[1] & Bruno Moulin[6]

1 Centre Universitaire des Maladies Rénales, CHU de Caen, Caen Cedex 9, France
2 Service de Néphrologie et Immunologie Clinique, CHRU Bretonneau, Tours, France
3 Service de Néphrologie – Transplantation, CHRU de Lille, Lille, France
4 Service de Néphrologie – Transplantation Adultes, Hôpital Universitaire Necker, Paris, France
5 U1086 Inserm, "ANTICIPE", Centre de Lutte Contre le Cancer François Baclesse, Caen Cedex 05, France
6 Service de Néphrologie et Transplantation, Hôpital Civil, Strasbourg, France

Correspondence
Valérie Chatelet, Néphrologie, CHU CAEN, Avenue de la Côte de Nacre, F 14000 Caen Cedex 9, France.
Tel.: +33 2 31 27 25 75;
fax: +33 2 31 27 24 73;
e-mail: chatelet-v@chu-caen.fr

SUMMARY

Transplant center organization, that is a modifiable factor, may affect the access to living-donor kidney transplantation (LDKT). The objective of this study was to identify the center characteristics associated with LDKT using a hierarchical analysis. This was a retrospective multicenter observational study of 8701 patients who received a first renal graft between 2010 and 2014 in 32 transplantation centers of France. Hierarchical modeling was used to estimate the center effect and organization associated with LDKT. Among 8507 patients, 1225 (12%) were transplanted with a LD kidney. There was a transplant center effect on the proportion of LDKT. After adjustment for patient and center characteristics, the random effect variance decreased by 47%. Patients transplanted at a center with more than four nephrologists [1.81 (95% CI: 1.10–2.95)] and more than 1.5 nurse transplant coordinators [1.98 (95% CI: 1.26–3.13)] were more likely to be transplanted with a LD kidney. ABO-incompatible program was associated with LDKT [2.23 (95% CI: 1.22–4.06)]. There was a transplant center effect on the proportion of LDKT that could be decreased by modifiable center characteristics. Our study suggests the importance of the transplant team organization on the LDKT utilization.

Transplant International 2019; 32: 865–875

Key words
center effect, living-donor kidney transplantation, renal transplantation, socioeconomic inequalities

Received: 7 November 2018; Revision requested: 7 January 2019; Accepted: 19 March 2019;
Published online: 2 April 2019

Introduction

Living-donor kidney transplantation (LDKT) is the optimal treatment for end-stage kidney disease in patients with no contraindications [1]. LDKT patients have a better quality of life than deceased donor transplant patients. LDKT is also a response to the shortage of organs from deceased donors [2,3] and it minimizes the time spent on dialysis [4]. LDKT is associated with longer dialysis-free survival compared with deceased donor transplantation [5]. Consequently, access to living-donor transplantation is a concern for nephrologists in charge of end-stage renal disease patients and for the transplant teams. In France, LDKT represents only 16% of the kidney transplants [6] whereas the proportions of LDKT can reach 30–40% in other developed countries [7–9]. Thus, measures should be implemented to increase the proportion of LDKT in France. Discrepancies regarding LDKT could be explained by patient characteristics and by ethnic and socioeconomic disparities [10]. In the United States, ethnic disparities, which are often associated with social deprivation, are

doi:10.1111/tri.13429

associated with access to LDKT [11,12]. Patients' referral to the transplant center by dialysis facilities could affect the proportion of LKDT. Kidney transplantation strategies, such as ABO-incompatible transplantation, can increase LDKT. Hall *et al.* [11] suggested that transplant centers' experience is associated with a higher proportion of LDKT. At the transplant center level, organization and practice are modifiable factors that may also influence the proportion of LDKT. To the best of our knowledge, there are no published data available about the effect of transplant center organization on the proportion of LDKT using a statistical method that allows assessment of the magnitude of the center effect and the identification of factors that could decrease the heterogeneity between facilities [13]. We hypothesize that center organization influences the proportion of LDKT. The objective of this study was to estimate the center effect on the proportion of living kidney transplantation and to identify which center characteristics were associated with the use of LDKT using a hierarchical analysis.

Materials and methods

Study population

This was a retrospective study using data from the Cristal database of the Agence de la Biomédecine, where data from transplanted patients at the 32 French transplantation centers are registered. Patients older than 18 years who underwent their first renal transplant from either a living or deceased donor in France between January 1, 2010 and December 31, 2014 were included in the study. We excluded patients who underwent multiorgan transplantation and those with a liver or cardiac transplant. The observation period ended on June 1, 2016. There were 9205 transplanted patients in the original dataset. Of these 9205 patients, 8701 patients had a precise home address (required for the European Deprivation Index calculation) that had been entered into the database at the time of registration on the waiting list who formed the final dataset.

Definition of variables

Event of interest

The event of interest was kidney transplantation with a living-donor kidney among the population of first renal transplant recipients in France during the study period. The comparator was the deceased donor transplantation. Only patients receiving a first renal transplantation were included in this study to avoid intra-cluster correlation in the hierarchical analysis.

Individual characteristics (level 1 covariates)

Patient characteristics were extracted from the Cristal database of the French Agence de la Biomédecine. In France, patients are registered on the waiting list even if a living-donor transplantation is planned. The following patient characteristics at registration on the waiting list were noted: age, sex, underlying nephropathy, diabetes mellitus, cardiovascular disease (coronaropathy, myocardial infarction, chronic heart failure, angiopathy, and stroke), chronic pulmonary disease, body mass index (BMI), tobacco use, dialysis modality (peritoneal dialysis or hemodialysis), hepatitis C virus (HCV) infection, and preemptive registration. We also collected the preemptive transplantation status, pre-transplant dialysis duration which was divided into tertiles and a category was added for preemptive transplant patients. The European Deprivation Index (EDI) was calculated using the patient's home address at registration for the waiting list [14]. Subsequently, the EDI was separated in two categories (quintile 5, which is the most deprived patients, versus other quintiles), since 32% of the transplanted patients were classified in the quintile 5 of the population in one recent study from our group [15]. The EDI was calculated for each patient then subjects were separated in five groups based on the EDI quintiles determined in the French population.

Center characteristics (level 2 covariates)

In France, transplantation is only performed in academic hospitals. There is one renal transplant center by academic hospital that performs organ transplantation. A survey about center organization was conducted by the transplantation committee of the French Society of Nephrology Dialysis and Transplantation (SFNDT) in 2017. A questionnaire about the center organization and the center characteristics during the study period was completed by the transplant program medical director for each kidney transplant team in France. The following data regarding the center were collected: the number of kidney transplants by center and by year during the study period, the number of senior nephrologists by center (fellow and junior staff were not considered as senior physician), the number of transplant nurse coordinators by center; the number of senior surgeons by center, ABO or HLA-incompatible program in the center; operating room or an intensive care unit dedicated in the center.

Transplant International 2019; 32: 865–875

Statistical analysis

The distribution of categorical covariates was described by frequencies and percentages, while that of continuous covariates was described by median (first and third quartile or extreme values). The event of interest was living donor kidney transplantation. A bivariable analysis was performed to estimate the association between each covariate and LDKT with a logistic regression model. The functional form of the quantitative predictor was assessed using regression splines. Continuous variables were separated into categories when there was no linear relationship between the predictor and the logit of event of interest. Cook distance represents numerically the level of modification of model coefficients when a given subject is dropped from the data set. When there was an important modification in the bivariable analysis the subject was considered "influent" and it was verified that the observation did not correspond to impossible values or to errors in data capture.

Hierarchical modeling was used to assess which patient and center characteristics were associated LDKT [13,16,17]. A multilevel regression logistic model was used for the analysis. The center effect on the use of LDKT was estimated by the random effect variance. Patient and center characteristics were selected for the multilevel multivariable analysis if the p-value was <0.20 in the bivariable analysis. An empty model (model 0), with the center as a random effect, was compared with a logistic empty model to detect the center effect. Because the center effect was significant, logistic regression modeling was performed with the center as a random effect and patient characteristics (level 1), center organization, and center characteristics (level 2) as fixed effects [13]. To quantify the heterogeneity between centers, we calculated the intraclass correlation coefficient (ICC) also called variance partition coefficient (VPC). Intraclass correlation coefficient represents the proportion of the total variance of the outcome attributed to the center level. Intraclass correlation coefficient was estimated with the latent variable method, that is $ICC = VA/(VA + \pi^2/3)$, where VA is the variance of the random effect and $\pi^2/3$ is the variance of the underlying standard logistic error. To estimate the contribution of the covariates introduced in each model, proportional change in variance (PCV) was calculated [PCV = (VN1 − VN2)/VN1, where VN1 is the variance of random effect of the empty model and VN2 is the level-2 variance of the model 1 or of the model 2].

Individual covariates were included in the model to investigate whether center heterogeneity was explained by the patient composition of the center. Subsequently, center covariates were included to investigate if the center effect was influenced by center characteristics and organization.

The Cristal database has the approval of the French national ethics committee "commission Nationale de l'Informatique et des Libertés". This study was conducted within the framework of this authorization that includes ethical consideration.

Statistical analyses were performed using R 3.1.2. (R Foundation for Statistical Computing, Vienna, Austria), including the lme4, lattice, and nnet packages.

Missing data

The proportion of missing data was 10% for the cardiovascular status, 7% for diabetes, and 2% for HCV. There were no missing data neither for the outcome nor for the center characteristics (level 2 covariate). Multiple imputation using the chained equation was performed with every recipients' characteristics.

Results

Patient and center characteristics by type of transplantation

Of the 8507 incident transplant patients, 1225 (12%) were transplanted using a kidney from a living donor. There was no statistical difference regarding the patients' characteristics between individuals excluded because of missing address and the other patients (age, gender, BMI, comorbid condition, nephropathy, HCV status, dialysis modality). Compared with the patients transplanted with a deceased donor, patients who received a kidney from a living donor were younger (46 vs. 57 years), more frequently male (67% vs. 63%), and had less comorbid conditions (diabetes, 8% vs. 18%; cardiovascular disease, 13% vs. 25%; HCV, 2% vs. 3%). There was a difference in the underlying nephropathy distribution between the two groups. There were more patients exposed to social deprivation among those transplanted with a kidney from a deceased donor compared with those who received a kidney from a living donor (quintile 5 of the EDI: 33% vs. 27%). The preemptive transplantation proportion was higher in the living-donor group compared with the deceased donor group (39% vs. 12%). Patient characteristics are presented in Table 1.

Among the transplant centers, 22 (68.7%) had an operating room dedicated to transplantation, and seven

Table 1. Patient characteristics by type of donor.

Patient characteristics	Deceased donor *N* = 7476 (88%)	Living donor *N* = 1225 (12%)
	Median (IQR)	**Median (IQR)**
Age (years)	57 [47–65]	46 [34–56]
	***N* (%)**	***N* (%)**
Gender (male)	4733 (63)	818 (67)
BMI (kg/m^2)		
<20	197 (3)	50 (4)
[20–25]	3533 (47)	670 (55)
>25	3746 (50)	505 (41)
Diabetes	1367 (18)	99 (8)
Cardiovascular disease	1876 (25)	165 (13)
Hepatitis C	203 (3)	19 (2)
Nephropathy		
Diabetic	831 (11)	64 (5)
Glomerulonephritis	1611 (22)	368 (30)
Interstitial nephritis	690 (9)	99 (8)
PKD	1406 (19)	244 (20)
Systemic disease	257 (3)	45 (4)
Uropathy	148 (2)	56 (5)
Vascular	787 (11)	79 (6)
Miscellaneous	401 (5)	76 (6)
Unknown	1345 (18)	194 (16)
Dialysis modality at registration (PD)	794 (12)	127 (17)
EDI (quintile 5, most deprived)	2492 (33)	326 (27)
Pre-emptive registration	2350 (31)	676 (55)
Pre-emptive transplantation	886 (12)	475 (39)
Duration on dialysis (months)		
Preemptive	886 (12)	475 (39)
Tertile 1]0.03–18.50]	1980 (26)	445 (36)
Tertile 2]18.50–37.40]	2217 (30)	203 (17)
Tertile 3]37.40–395.00]	2393 (32)	102 (8)
HLA class I antibody > 0%	1740 (26)	236 (24)
HLA class I antibody > 0%	1090 (17)	155 (17)

BMI, body mass index; EDI, European Deprivation Index; HLA, human leukocyte antigen.

(21.7%) had an intensive care unit for transplanted patients. There were 27 (84%) centers with an ABO-incompatible transplant program and 20 (62%) that had an HLA-incompatible transplant program. The median number of nephrologists on the transplant team was two, and the median number of senior surgeons was three. Center characteristics are displayed in Table 2.

Bivariable analysis

Living-donor transplantation was associated with recipient age, male sex, and BMI. Diabetics, patients with a cardiovascular disease, and those who were seropositive for HCV were less likely to be transplanted with a kidney from a living donor. There was an association between the underlying nephropathy and the chance of being transplanted with a living-donor kidney (*P* global <0.05). Social deprivation was associated with a lower probability of being transplanted with a living-donor kidney for the quintile 5 of the EDI compared with the other quintiles as a reference class. There was a greater proportion of preemptive transplantation in the living transplantation group. HLA mismatch was associated with living-donor transplantation.

There was a significant association between the transplant team characteristics and living transplantation. This is because patients transplanted by a team with more than four nephrologists, more than five senior surgeons, and more than 1.5 transplant coordinators had a greater probability of being transplanted with a living-donor kidney. The volume of the center activity

Transplant International 2019; 32: 865–875

Table 2. Transplant center characteristics.

	Median (extreme values)
Senior nephrologists in the transplant team	2 (0.5–4)
Transplant coordinators in the transplant team	3 (1–8)
	Number (%)
Senior surgeons in the transplant team	
Tertile 1]2–5]	14/31 (45.2)
Tertile 2]5–7]	10/31 (32.2)
Tertile 3]7–12]	7/31 (22.6)
Center with ABO-incompatible transplantation program	27/32 (84.4)
Center with HLA-incompatible transplantation program	20/32 (62.5)
Center size (number of transplantations per year)	
≤70	10/32 (31.2)
[70–150]	16/32 (50)
>150	6/32 (18.7)
Center with an operating room dedicated to transplantation	7/32 (21.8)
Center with intensive care unit dedicated to transplantation	22/32 (68.7)

HLA, human leukocyte antigen.

and an operating room dedicated to transplantation were also associated with the type of kidney donation whereas there was no association between the intensive care unit for transplantation and the type of organ donation. Patients who underwent kidney transplantation at centers with either an ABO or HLA-incompatible program were more likely to receive a kidney from a living donor. The results of the bivariable analysis are displayed in Table 3.

Multivariable analysis (hierarchical modeling)

Center effect

The random effect variance was 0.32 in model 0, and the ICC was 0.13. This means that there was a significant variation across transplant centers regarding the odds of undergoing a living-donor transplantation. The random effect variance did not decrease after adjusting for patient characteristics (0.49) and the type of transplantation (preemptive or transplantation on dialysis). However, after adjusting for patient characteristics and center characteristics, the random effect variance decreased significantly (percentage of variance change, 47%). The ICC was 0.05%, indicating that the variance of the center effect was almost fully explained by the center characteristics collected in our study.

The center effect (adjusted and nonadjusted on the patients' and centers' characteristics) is presented in Fig. 1.

Patient characteristics (level 1)

In the multivariable analysis, patient age, sex, diabetes, and underlying nephropathy were still associated with living-donor transplantation. Patients exposed to social deprivation were less likely to receive a kidney from a living donor [0.63 (95% CI: 0.54–0.74), for the patients in quintile 5 of the EDI compared with the other quintiles grouped in a single level].

Living-donor transplantation was associated with preemptive transplantation [5.03 (95% CI: 4.31–5.87), reference level: transplantation on dialysis].

Center characteristics (level 2)

Patients transplanted at a center with more than four nephrologists [1.81 (95% CI: 1.10–2.95)], and those transplanted at a center with more than 1.5 nurse transplant coordinators [1.98 (95% CI: 1.26–3.13)] were more likely to be transplanted with a living-donor kidney compared with the other patients. There was no association between the size of the surgical team and living-donor transplantation. Patients receiving a renal transplant in a center with an ABO-incompatible program had a higher chance of being transplanted with a living-donor kidney [2.23 (95% CI: 1.22–4.06)] compared with other centers. However, neither the center size nor the number of operating rooms dedicated to transplantation was associated with the likelihood of living-donor transplantation. When the time spent on the waiting list was entered in model 3 as an individual

Table 3. Bivariable analysis (logistic regression). Factors associated with living donor transplantation.

	OR (95% CI)	*P*-value
Patient characteristics		
Age (years)	0.95 (0.95–0.96)	<0.01
Gender (female)	0.86 (0.75–0.97)	0.02
BMI (kg/m^2)		
<20	1.34 (0.96–1.83)	0.07
[20–25]	ref	ref
>25	0.71 (0.63–0.80)	<0.01
Diabetes	0.39 (0.32–0.48)	<0.01
Cardiovascular disease	0.46 (0.39–0.55)	<0.01
Hepatitis C	0.56 (0.34–0.88)	0.02
Nephropathy		
Diabetic	0.44 (0.60–1.36)	<0.01
Glomerulonephritis	1.32 (0.88–1.32)	<0.01
Interstitial nephritis	0.83 (0.46–0.81)	0.14
PKD	ref	ref
Systemic disease	1.01 (0.71–1.41)	0.96
Uropathy	2.18 (1.55–3.04)	<0.01
Vascular	0.58 (0.44–0.75)	<0.01
Miscellaneous	1.09 (0.82–1.44)	0.54
Unknown	0.83 (0.68–1.02)	0.07
EDI (quintile 5)	0.73 (0.63–0.83)	<0.01
Pre-emptive transplantation	4.57 (3.99–5.22)	<0.01
HLA antibody class I > 0%	0.93 (0.80–1.09)	0.38
HLA antibody class II > 0%	1.00 (0.83–1.09)	0.96
Transplant center characteristics		
Center with more than 4 senior nephrologist	2.02 (1.72–2.37)	<0.01
Center with more than 1.5 transplant coordinator	1.98 (1.72–2.28)	<0.01
Number of senior surgeon in the transplant center		
Tertile 1]2–5]	ref	ref
Tertile 2]5–7]	1.51 (1.31–1.75)	<0.01
Tertile 3]7–12]	1.12 (0.96–1.31)	0.15
Center size (number of transplantation per year)		
≤70	ref	ref
[70–150]	1.92 (1.58–2.34)	<0.01
>150	2.35 (1.93–2.88)	<0.01
Center with ABO-incompatible transplantation program	2.54 (1.92–3.42)	<0.01
Center with HLA-incompatible transplantation program	1.70 (1.47–1.98)	<0.01
Center with an operating room dedicated to transplantation	1.31 (1.14–1.51)	<0.01
Center with an intensive care unit dedicated to transplantation	0.95 (0.83–1.09)	0.43

BMI, body mass index; EDI, European Deprivation Index; HLA, human leukocyte antigen.

variable, centers characteristics were still associated with the event of interest (data not shown).

The results of the multivariable analysis are displayed in Table 4.

Discussion

Our study demonstrates that, in France, there was heterogeneity between the 32 transplant centers regarding the proportion of LDKT. The ICC estimation showed that 9% of the variance in the proportion of LDKT could be attributed to the transplant center effect. This finding is a matter of concern because, in France, 16% of the renal transplants are performed using a living-donor kidney, which is lower than the proportion observed in other countries [9].

Center effect must be investigated because it allows implementation of measures at the center level that could improve patient care. Appropriate statistical methods are necessary to investigate the magnitude of

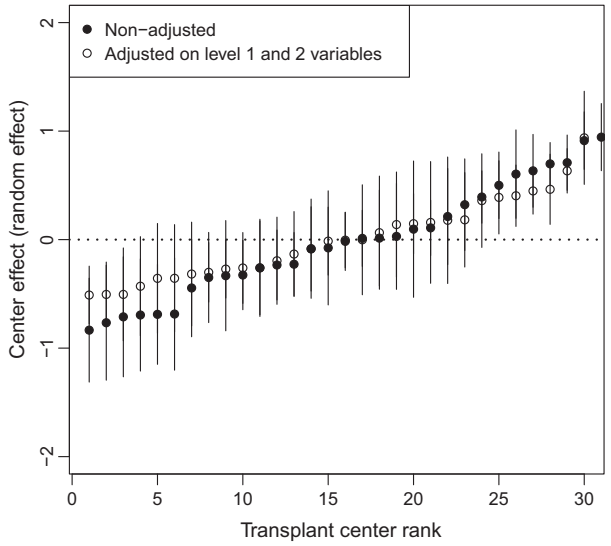

Figure 1 Random effect of each center nonadjusted and adjusted on the patients' and centers' characteristics (center ranked by the value of center effect).

the center effect and to identify which modifiable factor at the facility level could decrease the center effect [17]. Transplant center organization and practice may influence transplantation activity. To the best of our knowledge, studies about the center effect in the field of transplantation focused on the role of dialysis facility characteristics on access to the waiting list, and the outcome on transplantation [18–22].

In our study, the random effect did not vary significantly after adjustment for level 1 variables, indicating that the center effect was not influenced by differences in transplanted patient characteristics between the transplant centers. The heterogeneity between transplant centers decreased by 47% when center characteristics (level 2 variables) were entered into the multivariable analysis. At the center level, both the number of nephrologists on the renal transplant team and the number of nurse transplant coordinators were significantly associated with the proportion of LDKT. In the multivariable analysis, center size, which was measured by the number of transplants per year and per center, was not associated with LDKT.

In France as in others country, nurse transplant coordinators help both the donor and the recipient to navigate through the process that leads to renal transplantation. Patient education and information about LDKT is delivered by a nurse transplant coordinator [23]. The nurse transplant coordinator is also involved in evaluating living donors for organ donation [24]. The role of the nurse transplant coordinator may explain the higher chance of a patient being transplanted with a living-donor kidney in a center with more than one full time nurse transplant coordinator.

Living-donor kidney transplantation is a complex process where both the recipient and donor must be closely assessed before renal transplantation [6,25,26]. During donor recruitment, patient information on the potential short and long-term risks must be delivered by physicians with specific skills [26,27]. Additionally, it is the duty of the transplant team to obtain donor consent to enter into the procedure for donor medical assessment before transplantation, to evaluate the risk of organ donation, and to obtain the donor's agreement for organ donation. Consequently, sharing the responsibility in a group of nephrologists with knowledge and experience in transplantation could help physicians to make a joint decision. This could facilitate decision-making, reduce the evaluation time [28], and consequently increase the proportion of living-donor transplantation, independent of the center size. In support of this, one recent study where the evaluation time for living donors between Canadian and Australian transplantation centers was compared suggested that center level factors may influenced the duration of the living donor evaluation [28]. In a German study, authors reported that a multidisciplinary transplant team with a transplant coordinator improved the LDKT program [24].

Centers with an ABO-incompatible program had a greater proportion of LDKT compared with other centers in our study. An ABO-incompatible program increases the possibility that LDKT will be performed [29]. The ABO-incompatible program is also a proxy of the transplant center experience that may influence the proportion of LDKT. One study has suggested that the transplant center experience was associated with LDKT [11].

Patient referral to the transplant center may also partially explain the differences between the transplant centers. Although guidelines are available for transplant candidate assessment, it has been demonstrated that patient referral to the transplant center varies between dialysis centers [30]. One recent study from the United Kingdom, where dialysis centers were interviewed about their practice regarding patient assessment for renal transplant, showed wide variation between centers [31,32]. The Consensus Conference Workgroup proposed four recommendations to reduce the heterogeneity in access to LDKT, and one of these is based on a transplant liaison program to facilitate patient navigation from dialysis to transplant teams [33]. Transplant navigators can ensure the role of the transplant liaison

Table 4. Multivariable analysis (mixed logistic regression). Factors associated with living donor transplantation.

		Model 1		Model 2	
	Model 0 (empty model)	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Fixed effects					
Level 1: patient characteristics					
Age (years)	–	0.95 (0.95–0.96)	<0.01	0.95 (0.95–0.96)	<0.01
Gender (male)	–	1.22 (1.05–1.41)	<0.01	1.18 (1.02–1.37)	0.03
BMI (kg/m^2)					
<20	–	0.88 (0.61–1.28)	0.51	0.91 (0.62–1.34)	0.64
[20–25]	–	ref	ref	ref	ref
>25	–	1.00 (0.87–1.15)	0.97	1.03 (0.89–1.20)	0.64
Diabetes	–	0.71 (0.51–0.97)	0.03	0.70 (0.51–0.97)	0.03
Cardiovascular disease	–	0.85 (0.70–1.03)	0.09	0.85 (0.70–1.03)	0.11
Hepatitis C	–	0.69 (0.42–1.14)	0.15	0.62 (0.37–1.06)	0.08
Nephropathy					
Diabetic	–	0.90 (0.60–1.36)	0.63	0.97 (0.64–1.48)	0.90
Glomerulonephritis	–	1.08 (0.88–1.32)	0.47	1.14 (0.93–1.41)	0.20
Interstitial nephritis	–	0.61 (0.46–0.81)	<0.01	0.63 (0.47–0.85)	<0.01
PKD	–	ref	ref	ref	ref
Systemic disease	–	0.94 (0.65–1.38)	0.77	0.96 (0.65–1.42)	0.85
Uropathy	–	1.02 (0.68–1.53)	0.92	1.15 (0.65–1.42)	0.51
Vascular	–	0.77 (0.58–1.04)	0.09	0.82 (0.76–1.75)	0.19
Miscellaneous	–	0.90 (0.65–1.23)	0.50	0.95 (0.61–1.11)	0.76
Unknown	–	0.86 (0.68–1.08)	0.20	0.89 (0.69–1.31)	0.36
EDI (quintile 5)	–	0.63 (0.54–0.74)	<0.01	0.63 (0.54–0.74)	<0.01
Pre-emptive transplantation	–	5.03 (4.31–5.87)	<0.01	4.99 (4.26–5.85)	<0.01
Level 2: transplant center characteristics					
Center with more than four senior nephrologists	–	–		1.81 (1.10–2.95)	0.02
Center with more than 1.5 transplant coordinators	–	–		1.98 (1.26–3.13)	<0.01
Number of senior surgeon in the transplant center					
Tertile 1]2–5]	–	–		ref	ref
Tertile 2]5–7]	–	–		1.25 (0.80–1.96)	0.33
Tertile 3]7–12]	–	–		0.79 (0.47–1.33)	0.38
Center size (number of transplantation per year)					
≤70	–	–		ref	ref
[70–150]	–	–		0.95 (0.53–1.69)	0.85
>150	–	–		0.87 (0.40–1.89)	0.73
Center with an ABO-incompatible transplantation program	–	–		2.23 (1.22–4.06)	<0.01
Center with an operating room dedicated to transplantation	–	–		0.75 (0.47–1.20)	0.23
Random effects					
Variance	0.3284	0.4967		0.175	
ANOVA *P*-value	–	<0.01		<0.01	
ICC (%)	9.1	13.1		5.1	
PCV	–	−0.51		0.47	

BMI, body mass index; EDI, European Deprivation Index; ICC, intraclass coefficient correlation; PCV, proportional change in variance.

between dialysis facilities and transplant centers and can deliver information about the LDKT option [34].

As expected, patient characteristics (level 1 co-variables) were associated with the probability of LDKT. In our study, older patients had a lower risk of LDKT. It has been demonstrated that even elderly patients with a living donor had a lower chance of undergoing LDKT [10,35]. Sex was associated with LDKT in our study, a finding that is in agreement with other reports, which showed that women had a lower likelihood than men of undergoing a living-donor transplantation [36–38]. In contrast to the results of a recent study where obesity was a barrier for living-donor transplantation especially in women, BMI was not associated with LDKT in our analysis [39].

In the United Kingdom, ethnic disparities were associated with the use of LDKT among transplanted patients in the last report of the ATTOM study [40]. Social deprivation, which is often associated to ethnic disparities, was associated with the access to living-donor transplantation in different studies [11,12,40]. In our study, social deprivation, which was estimated using the European Deprivation Index (EDI), showed that the most deprived transplant patients had a lower risk of living-donor transplantation than the other patients [14].

Like in other studies, our report shows that pre-emptive transplantation was associated with living-donor allograft [10,40–42].

Our study has several limitations because residual confounders such as ethnic information (collecting data about ethnicity are not authorized in France) and consequently it was not possible to estimate the association between ethnicity and LDKT in our report. Furthermore, distance to the transplant center was not collected in the Cristal database. Additionally, the LDKT proportion was estimated among the transplant recipient population, and not in the end-stage renal disease patients. Dialysis facility referral for access to LDKT was not investigated in our results and could explain part of the disparities in access to LDKT. Whether, the center organization affects the proportion of LDKT or the proportion of LDKT has modified the center organization is a matter of concern. Nevertheless, it is interesting to notice that center organization *per se* was associated with LDKT independently of the center size. Moreover, although unlikely because of the hospital regulation, center organization may have changed during the study period. The status on the waiting list of the patients with a potential living donor may vary between centers, unfortunately, the survey of the Transplant Committee of the French Society of Nephrology, Dialysis and Transplantation did not address this issue. The mean time spent on the waiting list of each center may have biased the results. In France, the waiting time before transplantation differs from one region to another. One may speculate that at the region level the mortality rate, the health care organization, the number of intensive care unit, the willingness of the population to accept organ donation could influence the mean time on the waiting list at the center level. In addition, the GFR at registration on the waiting list differs between centers. LDKT could decrease the waiting time in some centers but on the contrary centers where the waiting time is long may have promoted living donation. The center organization could influence the time on the waiting list, but the time on the waiting list may also influence the center organization. Therefore, the mean time on the waiting list of the center probably aggregates other facility characteristics and further studies are needed to explore this aspect. However, it is important to notice that when the time spent on the waiting list was entered in the model as an individual characteristic it did not change the sense of the results.

In conclusion, this study shows that the heterogeneity in the use of LDKT between French transplant centers is influenced by the center resources such as the number of senior nephrologists, the number of nurse transplant coordinators, and the existence of an ABO-incompatible program. In view of our analysis, one may argue that the modification of the transplantation center organization could increase the proportion of LDKT. Our study suggests, in addition to other actions to promote renal transplantation, that measures should be implemented at the center level to increase the use of LDKT. Therefore, health authorities must consider the importance of transplant center organization when choosing how to distribute funding.

Authorship

VC and TL: performed the research, analysed data, collect data and wrote manuscript. PG: was in charge of the survey of the French Society of Nephrology Dialysis and Transplantation and reviewed the manuscipt. MH, DA and BM: reviewed the manuscipt. GL: performed the EDI calculation.

Funding

This study was funded by a grant from the Agence de la Biomédecine.

Conflict of interest

The authors have declared no conflict of interest.

Acknowledgements

We thank Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

REFERENCES

1. Tonelli M, Wiebe N, Knoll G, *et al.* Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant* 2011; **10**: 2093.
2. Cecka JM. Living donor transplants. *Clin Transpl* 1995: 363.
3. Roodnat JI, Van Riemsdijk IC, Mulder PG, *et al.* The superior results of living-donor renal transplantation are not completely caused by selection or short cold ischemia time: a single-center, multivariate analysis. *Transplantation* 2003; **12**: 2014.
4. Habbous S, McArthur E, Sarma S, *et al.* Potential implications of a more timely living kidney donor evaluation [Published online ahead of print 2018]. *Am J Transplant* 2018; **18**: 2719.
5. Matas AJ, Smith JM, Skeans MA, *et al.* OPTN/SRTR 2013 annual data report: kidney. *Am J Transplant* 2015; **15**(Suppl. 2): 1.
6. Le rapport médical et scientifique de L'Agence de la biomédecine 2016. *Agence de la Biomédecine*, 2017: 1.
7. McDonald SP, Russ GR. Australian registries-ANZDATA and ANZOD. *Transplant Rev* 2013; **2**: 46.
8. Matas AJ, Smith JM, Skeans MA, *et al.* OPTN/SRTR 2012 Annual data report: kidney. *Am J Transplant* 2014; **14**(Suppl. 1): 11.
9. Kramer A, Pippias M, Noordzij M, *et al.* The European Renal Association – European Dialysis and Transplant Association (ERA-EDTA) Registry annual report 2015: a summary. *Clin Kidney J* 2018; **1**: 108.
10. Gore JL, Danovitch GM, Litwin MS, Pham PT, Singer JS. Disparities in the utilization of live donor renal transplantation. *Am J Transplant* 2009; **5**: 1124.
11. Hall EC, James NT, Garonzik Wang JM, *et al.* Center-level factors and racial disparities in living donor kidney transplantation. *Am J Kidney Dis* 2012; **6**: 849.
12. Gill J, Dong J, Rose C, Johnston O, Landsberg D, Gill J. The effect of race and income on living kidney donation in the United States. *J Am Soc Nephrol* 2013; **11**: 1872.
13. Merlo J, Yang M, Chaix B, Lynch J, Rastam L. A brief conceptual tutorial on multilevel analysis in social epidemiology: investigating contextual phenomena in different groups of people. *J Epidemiol Community Health* 2005; **59**: 729.
14. Pornet C, Delpierre C, Dejardin O, *et al.* Construction of an adaptable European transnational ecological deprivation index: the French version. *J Epidemiol Community Health* 2012; **66**: 982.
15. Chatelet V, Bayat-Makoei S, Vigneau C, Launoy G, Lobbedez T. Renal transplantation outcome and social deprivation in the French healthcare system: a cohort study using the European Deprivation Index. *Transpl Int* 2018; **31**: 1089.
16. Merlo J, Chaix B, Yang M, Lynch J, Rastam L. A brief conceptual tutorial on multilevel analysis in social epidemiology: associationing the statistical concept of clustering to the idea of contextual phenomenon. *J Epidemiol Community Health* 2005; **59**: 443.
17. Tsampalieros A, Knoll GA, Fergusson N, Bennett A, Taljaard M, Fergusson D. Center variation and the effect of center and provider characteristics on clinical outcomes in kidney transplantation: a systematic review of the evidence. *Can J Kidney Health Dis* 2017; **4**: 1.
18. Kim SJ, Schaubel DE, Jeffery JR, Fenton SS. Centre-specific variation in renal transplant outcomes in Canada. *Nephrol Dial Transplant* 2004; **7**: 1856.
19. Elinder CG, Ekberg H, Bárány P, *et al.* Variations in graft and patient survival after kidney transplantation in Sweden: caveats in interpretation of center effects when benchmarking. *Transpl Int* 2009; **11**: 1051.
20. Zenios S, Atias G, McCulloch C, Petrou C. Outcome differences across transplant centers: comparison of two methods for public reporting. *Clin J Am Soc Nephrol* 2011; **12**: 2838.
21. Ravanan R, Udayaraj U, Ansell D, *et al.* Variation between centres in access to renal transplantation in UK: longitudinal cohort study. *BMJ* 2010; **341**: 1.
22. Paul S, Plantinga LC, Pastan SO, Gander JC, Mohan S, Patzer RE. Standardized transplantation referral ratio to assess performance of transplant referral among dialysis facilities. *Clin J Am Soc Nephrol* 2018; **2**: 282.
23. Rudow DL. Development of the center for living donation: incorporating the role of the nurse practitioner as director. *Prog Transplant* 2011; **4**: 312.
24. Fonouni H, Golriz M, Mehrabi A, *et al.* The role of an interdisciplinary transplant team on living donation kidney transplantation program. *Transplant Proc* 2010; **1**: 137.
25. Delmonico F; Council of the Transplantation Society. A report of the Amsterdam forum on the care of the live kidney donor: data and medical guidelines. *Transplantation* 2005; **79**: S53.
26. Lentine KL, Kasiske BL, Levey AS, *et al.* KDIGO clinical practice guideline on the evaluation and care of living kidney donors. *Transplantation* 2017; **101**: S1.
27. Grams ME, Sang Y, Levey AS, *et al.* Kidney-failure risk projection for the living kidney-donor candidate. *N Engl J Med* 2016; **5**: 411.
28. Habbous S, Arnold J, Begen MA, *et al.* Duration of living kidney transplant donor evaluation: finding from 2 multicenter cohort studies. *Am J Kidney Dis* 2018; **72**: 483.
29. Reese PP, Feldman HI, Bloom RD, *et al.* Assessment of variation in live donor kidney transplantation across transplant centers in the United States. *Transplantation* 2011; **12**: 1357.
30. Patzer RE, Plantinga LC, Paul S, *et al.* Variation in dialysis facility referral for kidney transplantation among patients with end-stage renal disease in Georgia. *JAMA* 2015; **6**: 582.
31. Kim JJ, Basu M, Plantinga L, *et al.* Awareness of racial disparities in kidney transplantation among health care providers in dialysis facilities. *Clin J Am Soc Nephrol* 2018; **13**: 772.
32. Pradel FG, Suwannaprom P, Mullins CD, Sadler J, Bartlett ST. Short-term impact of an educational program promoting live donor kidney transplantation in dialysis centers. *Prog Transplant* 2008; **4**: 263.

33. Rodrigue JR, LaPointe Rudow D, Hays R, American Society of Transplantation. Living donor kidney transplantation: best practices in live kidney donation–recommendations from a consensus conference. *Clin J Am Soc Nephrol* 2015; **9**: 1656.
34. Sullivan C, Leon JB, Sayre SS, *et al.* Impact of navigators on completion of steps in the kidney transplant process: a randomized, controlled trial. *Clin J Am Soc Nephrol* 2012; **10**: 1639.
35. Weng FL, Reese PP, Mulgaonkar S, Patel AM. Barriers to living donor kidney transplantation among black or older transplant candidates. *Clin J Am Nephrol* 2010; **12**: 2338.
36. Couchoud C, Bayat S, Villar E, Jacquelinet C, Ecochard R, REIN registry. A new approach for measuring gender disparity in access to renal transplantation waiting lists. *Transplantation* 2012; **5**: 513.
37. Kayler LK, Meier-Kriesche HU, Punch JD, *et al.* Gender imbalance in living donor renal transplantation. *Transplantation* 2002; **2**: 248.
38. Bromberger B, Spragan D, Hashmi S, *et al.* Pregnancy-induced sensitization promotes sex disparity in living donor kidney transplantation. *J Am Soc Nephrol* 2017; **10**: 3025.
39. Gill JS, Hendren E, Dong J, Johnston O, Gill J. Differential association of body mass index with access to kidney transplantation in men and women. *Clin J Am Soc Nephrol* 2014; **5**: 951.
40. Wu DA, Robb ML, Watson CJE, *et al.* Barriers to living donor kidney transplantation in the United Kingdom: a national observational study. *Nephrol Dial Transplant* 2017; **5**: 890.
41. Kasiske BL, London W, Ellison MD. Race and socioeconomic factors influencing early placement on the kidney transplant waiting list. *J Am Soc Nephrol* 1998; **11**: 2142.
42. Kasiske BL, Snyder JJ, Matas AJ, Ellison MD, Gill JS, Kausz AT. Preemptive kidney transplantation: the advantage and the advantaged. *J Am Soc Nephrol* 2002; **5**: 1358.