

Facilitating access to the renal transplant waiting list does not increase the number of transplantations: comparative study of two French regions

Mathilde Lefort, Cécile Vigneau, Annelen Laurent, Saïd Lebbah, Nolwenn Le Meur, Jean-Philippe Jais, Eric Daugas, Sahar Bayat

▶ To cite this version:

Mathilde Lefort, Cécile Vigneau, Annelen Laurent, Saïd Lebbah, Nolwenn Le Meur, et al.. Facilitating access to the renal transplant waiting list does not increase the number of transplantations: comparative study of two French regions. Clinical Kidney Journal, 2016, 9 (6), pp.849-857. 10.1093/ckj/sfw078. hal-01439362

HAL Id: hal-01439362 https://univ-rennes.hal.science/hal-01439362

Submitted on 8 Jun 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.







Clinical Kidney Journal, 2016, vol. 9, no. 6, 849-857

doi: 10.1093/ckj/sfw078

Advance Access Publication Date: 9 September 2016 Original Article

Facilitating access to the renal transplant waiting list does not increase the number of transplantations: comparative study of two French regions

Mathilde Lefort¹, Cécile Vigneau², Annelen Laurent¹, Saïd Lebbah³, Nolwenn Le Meur¹, Jean-Philippe Jais³, Eric Daugas⁴ and Sahar Bayat ¹

¹EHESP, Sorbonne Paris Cité, METIS, Avenue du professeur Léon Bernard, 35043 Rennes, France, ²CHU Pontchaillou, Service de Néphrologie, Rennes, France, ³Université Paris Descartes, Sorbonne Paris Cité, INSERM UMRS 1138 team 22; CHU Necker-Enfants Malades, Biostatistics Unit, Paris, France, and ⁴Hôpital Bichat – Claude-Bernard, Service de Néphrologie, Université Paris Diderot, DHU FIRE, INSERM U1149, Paris, France

Correspondence and offprint requests to: Mathilde Lefort; E-mail: mathilde.lefort@ehesp.fr

Abstract

Background: In France, there are important regional disparities of access to the renal transplant waiting list and transplantation. Our objectives were to compare the characteristics of patients with end-stage renal disease (ESRD) of two French regions (Ile-de-France and Bretagne) and to identify determinants of access to the waiting list and subsequent transplantation, with a focus on temporary inactive status (TIS) periods.

Methods: All 18–80-year-old incident patients who started dialysis in Ile-de-France or Bretagne between 2006 and 2009 were included (n = 6160). Associations between patients' characteristics and placement on the waiting list or transplantation were assessed using a Fine and Gray model to take into account the competing risk of death and living donor transplantation.

Results: At the end of the follow-up (31 December 2013), more patients had undergone transplantation in Bretagne than in Ilede-France (30 versus 27%), although the percentage of waitlisted patients was higher in Ile-de-France than in Bretagne (47 versus 33%). More patients were on TIS and with a longer median TIS duration in Ile-de-France. Independent of age and clinical characteristics, patients in Bretagne were less likely to be waitlisted than those in Ile-de-France [subdistribution hazard ratio 0.77 (95% confidence interval 0.7–0.9)]. After waitlisting, patients in Bretagne were four times more likely to be transplanted.

Conclusions: Our study highlights clinical practice differences in Bretagne and Ile-de-France and shows that facilitating access to the waiting list is not sufficient to improve access to renal transplantation, which also depends on organ availability.

Key words: chronic renal failure, dialysis, end-stage renal disease, epidemiology, kidney transplantation

Introduction

End-stage renal disease (ESRD) management is an important public health issue. Patients with ESRD need renal replacement therapy (haemodialysis, peritoneal dialysis or renal transplantation) to improve their survival. Renal transplantation is associated with better survival [1-3], better quality of life [4, 5] and lower cost [6] compared with dialysis. However, access to renal transplantation is often limited by organ shortage [7]. Previous studies found disparities in the access and evaluation of candidates for renal transplantation [8-13].

In France, the first step towards renal transplantation is placement on the French national renal transplant waiting list, which is managed by the Agence de la Biomédecine (ABM). Patients are placed on the list by a nephrologist after assessment of their medical status. Placement on the waiting list depends on the clinical team's practices, which may not be homogeneous between regions or even between transplant centres in the same region. Before the national guidelines, established by the Haute Autorité de Santé (French national health agency) in October 2015 [14], only European recommendations on the evaluation of patients to be placed on the list were used [15, 16].

After this first step, allocation of an organ from a deceased donor is based on the allocation score developed by ABM. This score includes the time on the waiting list, dialysis duration, age difference between the recipient and donor and donor-recipient immunological and biological compatibly (Supplementary data, Table S1). Its modulation was slightly different between regions and the grafts were allocated regionally until February 2015. Any waitlisted patient who is currently unavailable or unsuitable for transplantation is identified by a temporary inactive status (TIS) and cannot be transplanted. If the initial medical check-up is not finalized, this patient might be identified by an initial TIS period, although this does not correspond to a medical event limiting access to transplantation. Consequently, after placement on the waiting list, access to kidney transplantation depends on the allocation score, organ availability and also TIS.

A previous study in 11 French regions showed that after taking into account medical and non-medical factors, placement on the list was significantly associated with the region of residence, suggesting waitlisting practice differences [17]. For technical reasons, this study did not include the Ile-de-France region, where 18% of the French population live (INSEE). The cumulative incidence of placement on the waiting list in Ile-de-France is higher compared with other French regions, while the Bretagne region is in the average [18]. Therefore, the Ile-de-France and Bretagne regions are good candidates to study the variations of access to the waiting list. Nonetheless, the consequences of differences in waiting list access between regions in terms of eventual access to transplantation were not evaluated. Moreover, the link between TIS periods and access to renal transplantation have never been studied in France.

The objectives of this study were (i) to compare the characteristics of patients with ESRD in the Ile-de-France and Bretagne regions and (ii) to identify determinants of access to the renal transplant waiting list and renal transplantation, with a focus on TIS periods in these regions.

Materials and methods

Study population

All 18-80-year-old incident patients with ESRD who started dialysis between 1 January 2006 and 31 December 2009 in Bretagne and Ile-de-France were extracted from the Renal Epidemiology and Information Network registry, a tool for public health decision support, evaluation and research [19]. Patients who received pre-emptive renal transplantation were not included.

ESRD incidence, after standardization for gender and age, was 174 per million population (pmp) in Ile-de-France and 126 pmp in Bretagne in 2013 [20].

Collected data

Demographic and clinical data at first dialysis were extracted. Three demographic variables were taken into account: age group (18-39, 40-59, 60-69 and 70-80 years), gender and region of residence.

The following patients' clinical features at first dialysis (baseline) were studied: primary renal disease categorized in six groups [glomerulonephritis, pyelonephritis, diabetic nephropathy, hypertensive and vascular nephropathy, polycystic kidney disease and others (other causes and unknown)], modality and type of first dialysis (haemodialysis or peritoneal dialysis, emergency first dialysis and first dialysis session with a catheter), cardiovascular diseases (coronary artery disease, congestive heart failure, peripheral vascular disease, myocardial infarction, arrhythmia, aortic aneurism, cerebrovascular disease), diabetes, chronic respiratory disease, hepatic disease, active malignancy, physical disabilities (ambulation impairment, paraplegia or hemiplegia, member amputation, blindness) and HIV infection. Haemoglobin levels were categorized as <10, 10-12 and >12 g/dL. For waitlisted patients, the date of placement on the list, date of transplantation, blood group (A, B, O and AB), panel reactive antibody (PRA) level and TIS periods were recorded. If an inactive period was <75 days and started concomitantly with placement on the list (± 2 days), it was considered as the period of completion of all medical examinations that are required for renal transplantation candidates and not as a TIS. Organ availability was quantified as the mean number of deceased donors per million population between the year of placement on the list and the year of transplantation or last follow-up. Date of death was also included.

Statistical analysis

The patients' characteristics were described and compared using Pearson's χ^2 test. Continuous variables were expressed as mean ± standard deviation. Means were compared using a Student test and medians using a non-parametric equality-of-medians test. Missing data were systematically imputed using multiple imputation by chained equation (MICE) with 10 imputations and one cycle, because missing data concerned only the haemoglobin level [21].

The outcomes of interest were

- 1. Placement on the renal transplant waiting list, regardless of the donor type (living or deceased). Death before waitlisting was considered as a competing event. Patients pre-emptively placed on the list before the beginning of dialysis were considered to be waitlisted at dialysis start. Times to outcomes (death, waiting-list placement) were calculated from the date of first dialysis. Non-waitlisted living patients were censored at the end of the follow-up (31 December 2013).
- 2. Deceased donor renal transplantation after placement on the list. Death before transplantation and living donor transplantation were considered as competing events. Times to outcomes (death, transplantation) were calculated from the date of placement on the list. Non-transplanted living patients were censored at the end of the follow-up.

3. Deceased donor transplantation after first dialysis. Death before transplantation and living donor transplantation were considered as competing events. Times to outcomes (death, transplantation) were calculated from the date of first dialysis. Non-transplanted living patients were censored at the end of the follow-up.

The association between patients' characteristics (including the region of residence) and outcomes of interest was assessed using Fine and Gray univariate analyses [22]. Variables with a P-value < 0.20 were included in the multivariate analysis. A Pvalue <0.05 was considered statistically significant. Results were reported as subdistribution hazard ratios (SHRs) with 95% confidence intervals (CIs) and P-values. The cumulative incidence function (CIF) curve, which represents the probability of transplantation after taking into account the competing risk of death before transplantation and living donor transplantation, was also used to compare the two regions. Statistical analyses were performed with STATA 13 software.

Results

Patients' characteristics

Patients' characteristics. Table 1 presents the baseline characteristics of the 6160 incident patients who started dialysis in Bretagne (18%) or Ile-de-France (82%) between 1 January 2006 and 31 December 2009. Their mean age was 64.3 ± 13.9 years in Bretagne and 60.1 ± 15.1 years in Ile-de-France (P < 10^{-4}).

Significant differences were found in the percentage of patients with diabetes (28% in Bretagne and 39% Ile-de-France), an active malignancy (12% and 8%), a chronic respiratory disease (14% and 8%) and more than two cardiovascular diseases (29% and 19%) (P < 10^{-4} for all).

On 31 December 2013, 33% of patients in Bretagne and 47% in Ile-de-France were waitlisted (Figure 1). Among these patients, 18% were placed on the list at first dialysis or pre-emptively in Bretagne and 19% in Ile-de-France.

Characteristics of waitlisted patients. The gender of waitlisted patients (total number = 2748; 14% in Bretagne and 86% in Ile-de-France) was comparable between regions (Table 2). The mean age was 51.8 ± 13.0 years in Bretagne and 50.1 ± 13.1 in Ile-de-France (P = 0.016).

Diabetes and hepatic disease were significantly more frequent in Ile-de-France than in Bretagne (27% versus 18% of patients with diabetes and 5% versus 2% with hepatic disease, respectively).

Access to the renal transplant waiting list, TIS and access to deceased donor transplantation

Access to the renal transplant waiting list. In univariate analyses, age and most comorbidities, except HIV infection, limited access to the waiting list (Supplementary data, Table S2). Multivariate analyses (Table 3) confirmed that age was a limiting factor for placement. In addition, diabetic nephropathy was associated with a 47% lower chance of being waitlisted compared with polycystic kidney disease, whereas peritoneal dialysis was associated with a higher probability of placement on the list [SHR 1.26 (95% CI 1.1-1.4)]. The chance of being waitlisted was also lower for patients with diabetes (by 20%), with active malignancy (by 63%) and with more than three cardiovascular diseases (by 49%). Patients who had a first dialysis session with a catheter were less likely to be waitlisted [SHR 0.78 (95% CI 0.7-0.9)]. Finally, in the multivariate model, patients in Bretagne were 23% less likely to be placed on the list than patients in Ile-de-France [SHR 0.77, (95% CI 0.7-0.9)].

Temporary inactive status. Overall, 1488 waitlisted patients had at least one TIS (42% in Bretagne and 56% in Ile-de-France; $P < 10^{-4}$). The mean number of TIS periods was 2.4 per patient in Bretagne and 2.0 in Ile-de-France (P = 0.0002). The TIS median duration was 6 months in Bretagne and 9 months in Ile-de-France (P = 0.014). On average, TIS duration represented 52 and 41% of the time spent on the waiting list in Bretagne and Ile-de-France, respectively $(P < 10^{-4})$.

In addition, 1041 patients were initially waitlisted with a TIS that had a median duration of 4 months in Bretagne and 5 months in Ile-de-France (P = 0.011). Among these 1041 patients, 211 were waitlisted pre-emptively. For these patients, the median TIS duration was 6 months in both regions (P = 0.628).

Access to deceased donor transplantation after waitlisting. At the end of the follow-up, 89% of waitlisted patients underwent renal transplantation, 4% were dead and 0.8% had a living donor transplant in Bretagne compared with 58%, 8% and 8%, respectively, in

Univariate analyses (Supplementary data, Table S2) showed that, after placement on the waiting list, patients in the 70-80years age group had higher chances of undergoing transplantation. Diabetes, more than three cardiovascular diseases (compared with no cardiovascular disease) and hepatic disease were associated with a lower probability of transplantation. In the multivariate model (Table 3), patients in the 60-69 and 70-80-years age groups were more likely to undergo transplantation than 18-39-year-old patients. Diabetes [SHR 0.78 (95% CI 0.6-1)] and more than three cardiovascular diseases [SHR 0.63 (95% CI 0.4-0.9); compared with no cardiovascular disease] were significantly associated with a reduced likelihood of transplantation. The probability of transplantation was also reduced for patients with at least one TIS period (by 56%). In the multivariate model, patients in Bretagne were 4.52 times more likely to be transplanted than patients in Ile-de-France. Time spent on the waiting list before transplantation was shorter for patients in Bretagne than in Ile-de-France (CIF attained 50%, 12.7 months after placement on the list in Bretagne versus 45.4 months in Ile-de-France) (Supplementary data, Figure S1). This difference remained when only patients without TIS were considered (5.3 months in Bretagne and 33.9 months in Ile-de-France).

In the multivariate model taking into account organ availability (Supplementary data, Table S3), the greater the organ availability, the higher was the probability of transplantation. Nevertheless, after taking region into account, organ availability was not significantly associated with access to renal transplantation. This fact may be related to the greater level of organ availability in Bretagne during the study period.

Access to deceased donor transplantation after first dialysis. Overall, 30% of all incident patients (waitlisted and non-waitlisted) in Bretagne underwent renal transplantation compared with 27% in Ile-de-France. In univariate analyses (Supplementary data, Table S2) as in multivariate analyses (Table 3), old age and comorbidities, except HIV infection, were associated with a lower probability of transplantation after dialysis start. In the multivariate model, patients in Bretagne were 2.07 times more likely to undergo transplantation than patients in Ile-de-France.

Table 1. Characteristics of incident patients

	Patients' basel	ne characteristics	Patients placed on the list at the end of the follow-up, %			
	Bretagne n (%)	Ile de France n (%)		Bretagne	Ile de France	
	1118 (18.1)	5042 (81.9)	P-value	33.5	47.1	
Gender						
Female	435 (38.9)	1785 (35.4)	0.027	34.0	46.8	
Male	683 (61.1)	3257 (64.6)		33.2	47.2	
Age (years)	,	()				
18–39	78 (7)	602 (11.9)	<10 ⁻⁴	88.5	89.2	
40–59	288 (25.8)	1617 (32.1)		68.8	76.3	
60–69	246 (22)	1166 (23.1)		35.0	43.7	
70–80	506 (45.3)	1657 (32.9)		4.3	5.7	
Primary renal disease	300 (1 3.3)	1037 (32.3)		4.5	5.7	
Polycystic kidney disease	120 (10 7)	227 (6 5)	<10 ⁻⁴	72.5	83.5	
	120 (10.7)	327 (6.5)	<10			
Hypertensive and vascular nephropathy	263 (23.5)	1204 (23.9)		17.1	37.5	
Diabetic nephropathy	130 (11.6)	1305 (25.9)		26.9	33.5	
Glomerulonephritis	164 (14.7)	607 (12)		51.2	72.5	
Pyelonephritis	57 (5.1)	148 (2.9)		49.1	54.1	
Others	384 (34.3)	1451 (28.8)		25.0	47.7	
First modality of dialysis						
Haemodialysis	990 (88.6)	4634 (91.9)	<10 ⁻⁴	33.0	46.2	
Peritoneal dialysis	128 (11.4)	408 (8.1)		37.5	57.4	
Diabetes						
No	800 (71.6)	3084 (61.2)	<10 ⁻⁴	38.6	56.5	
Yes	318 (28.4)	1958 (38.8)		20.8	32.2	
Active malignancy	, ,	()				
No	988 (88.4)	4660 (92.4)	<10 ⁻⁴	36.6	49.5	
Yes	130 (11.6)	382 (7.6)	120	10.0	17.3	
Chronic respiratory disease	150 (11.0)	302 (7.0)		10.0	17.5	
No	965 (86.3)	4636 (91.9)	<10 ⁻⁴	36.7	49.4	
Yes	153 (13.7)	406 (8.1)	<10	13.7	20.0	
HIV infection	155 (15.7)	400 (0.1)		15./	20.0	
No	1112 (00 C)	4001 (07.0)	<10 ⁻⁴	33.5	46.5	
	1113 (99.6)	4901 (97.2)	<10			
Yes	5 (0.4)	141 (2.8)		40.0	65.2	
Hepatic disease		/>				
No	1058 (94.6)	4754 (94.3)	0.651	34.7	47.2	
Yes	60 (5.4)	288 (5.7)		13.3	45.5	
Physical disabilities						
0	949 (84.9)	4358 (86.4)	0.175	38.0	52.7	
≥1	169 (15.1)	684 (13.6)		8.3	11.0	
Cardiovascular disease						
0	552 (49.4)	3010 (59.7)	<10 ⁻⁴	52.4	59.7	
1	243 (21.7)	1055 (20.9)		21.0	36.2	
2	154 (13.8)	552 (10.9)		11.7	20.8	
≥3	169 (15.1)	425 (8.4)		10.1	18.4	
Haemoglobin (g/dL)	(- ,)	- (/				
10–12	429 (38.4)	1463 (29)	<10 ⁻⁴	35.9	48.1	
10	462 (41.3)	2176 (43.2)	110	30.1	46.6	
>12						
	178 (15.9)	774 (15.4)		39.9	50.8	
Missing	49 (4.4)	629 (12.5)		22.4	41.8	
Emergency first dialysis session	706 (71.0)	0064 (70.6)	4.0-4	07.4	40.7	
No	796 (71.2)	3961 (78.6)	<10 ⁻⁴	37.4	48.7	
Yes	322 (28.8)	1081 (21.4)		23.9	41.2	
First dialysis session with a catheter						
No	691 (61.8)	2582 (51.2)	<10 ⁻⁴	40.5	52.7	
Yes	427 (38.2)	2460 (48.8)		22.2	41.2	

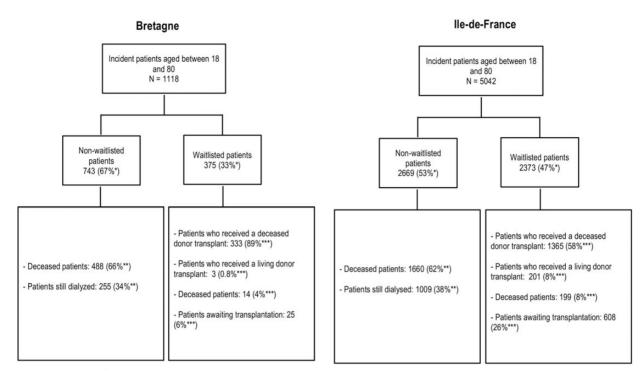
HIV, human immunodeficiency virus.

Discussion

This study compared access to the renal transplant waiting list and transplantation in two French regions (Bretagne and Ile-de-France) and shows that waitlisting strategies are stricter in

Bretagne than in Ile-de-France. Despite easier access to the waiting list, the likelihood of renal transplantation after dialysis start is reduced by half for patients in Ile-de-France. Indeed, once waitlisted, access to renal transplantation outweighed the reduced

P values highlighted in bold correspond to P<0.05 (P values statistically significant)



*Ratio based on incident patients, **Ratio based on non-waitlisted patients, *** Ratio based on waitlisted patients

Fig. 1. Summary of the patients' status in Ile-de-France and Bretagne at the end of the follow-up (31 December 2013).

Table 2. Characteristics of patients placed on the waiting list

	Baseline chara	acteristics of patients p	Deceased donor-transplanted patients at the end of the follow-up, %		
	Bretagne n (%) 375 (13.6)	Ile de France n (%) 2373 (86.4)	P-value	Bretagne 88.8	Ile de France 57.5
Gender					
Female	148 (39.5)	836 (35.2)	0.112	39.9	35.9
Male	227 (60.5)	1537 (64.8)		60.1	64.1
Age (years)	, ,	, ,			
18–39	69 (18.4)	537 (22.6)	0.123	19.2	23.0
40–59	198 (52.8)	1233 (52)		52.0	50.2
60–69	86 (22.9)	509 (21.4)		22.5	21.8
70–80	22 (5.9)	94 (4)		6.3	5.0
Primary renal disease					
Polycystic kidney disease	87 (23.2)	273 (11.5)	<10^4	24.9	14.5
Hypertensive and vascular nephropathy	96 (25.6)	692 (29.2)		25.5	27.3
Diabetic nephropathy	35 (9.3)	437 (18.4)		8.4	17.0
Glomerulonephritis	45 (12)	451 (19)		10.5	19.3
Pyelonephritis	84 (22.4)	440 (18.5)		22.5	18.9
Others	28 (7.5)	80 (3.4)		8.1	3.0
First modality of dialysis					
Haemodialysis	327 (87.2)	2139 (90.1)	0.081	86.5	90.1
Peritoneal dialysis	48 (12.8)	234 (9.9)		13.5	9.9
Diabetes					
No	309 (82.4)	1742 (73.4)	<10^-4	84.7	76.1
Yes	66 (17.6)	631 (26.6)		15.3	23.9
Active malignancy					
No	362 (96.5)	2307 (97.2)	0.46	97.3	97.7
Yes	13 (3.5)	66 (2.8)		2.7	2.3

Table 2. Continued

	Baseline chara	acteristics of patients p	Deceased donor-transplanted patients at the end of the follow-up, %			
	Bretagne n (%) 375 (13.6)	Ile de France n (%) 2373 (86.4)	P-value	Bretagne 88.8	Ile de France 57.5	
Chronic respiratory disease						
No	354 (94.4)	2292 (96.6)	0.037	95.8	97.2	
Yes	21 (5.6)	81 (3.4)		4.2	2.8	
HIV infection						
No	373 (99.5)	2281 (96.1)	0.001	99.4	97.5	
Yes	2 (0.5)	92 (3.9)		0.6	2.5	
Hepatic disease	. ,					
No	367 (97.9)	2242 (94.5)	0.005	97.9	95.2	
Yes	8 (2.1)	131 (5.5)		2.1	4.8	
Physical disabilities	. ,	, ,				
0	361 (96.3)	2298 (96.8)	0.56	97.3	97.6	
≥1	14 (3.7)	75 (3.2)		2.7	2.4	
Cardiovascular disease	, ,	` '				
0	289 (77.1)	1798 (75.8)	0.422	79.3	78.4	
1	51 (13.6)	382 (16.1)		13.2	14.9	
2	18 (4.8)	115 (4.8)		3.9	4.3	
≥3	17 (4.5)	78 (3.3)		3.6	2.4	
Haemoglobin (g/dL)	(/	()				
10–12	154 (41.1)	704 (29.7)	0.001	40.8	30.5	
<10	139 (37.1)	1013 (42.7)		36.3	40.6	
>12	71 (18.9)	393 (16.6)		19.5	18.3	
Missing	11 (2.9)	263 (11.1)		3.3	10.5	
Emergency first dialysis session	()	()				
No	298 (79.5)	1928 (81.2)	0.414	80.8	81.6	
Yes	77 (20.5)	445 (18.8)	0.111	19.2	18.4	
First dialysis session with a catheter	77 (2013)	113 (10.0)		13.2	10.1	
No	280 (74.7)	1360 (57.3)	<10 ⁻⁴	76.9	61.2	
Yes	95 (25.3)	1013 (42.7)	120	23.1	38.8	
TIS	33 (23.3)	1015 (12.7)		23.1	30.0	
No	218 (58.1)	1042 (43.9)	<10 ⁻⁴	63.7	52.6	
Yes	157 (41.9)	1331 (56.1)	110	36.3	47.4	
Blood groups	157 (11.5)	1551 (50.1)		50.5	17.1	
O	174 (46.4)	1048 (44.2)	0.269	46.2	38.5	
A	142 (37.9)	854 (36)	0.207	39.0	44.7	
В	44 (11.7)	370 (15.6)		11.1	11.0	
AB	15 (4)	101 (4.3)		3.6	5.8	
PRA level	12 (4)	101 (4.3)		3.0	٥.٥	
<85%	360 (96)	2133 (89.9)	<10 ⁻⁴	96.4	91.9	
<85% ≥85%	, ,	, ,	<10	3.6	91.9 8.1	
≥03/0	15 (4)	240 (10.1)		3.0	0.1	

HIV, human immunodeficiency virus; TIS, temporary inactive status; PRA: panel reactive antibody.

access to the waiting list in Bretagne, where patients were 4.5 times more likely to undergo transplantation and also more rapidly (3.6 times shorter waiting time). This is also the first study in France on TIS and its association with transplantation. In Ile-de-France, more patients had at least one TIS period and TIS cumulative duration was longer. However, relative to the overall time on the waiting list, waitlisted patients in Bretagne spent more time on TIS. These findings highlight differences of practice patterns and variations of access to renal transplantation in these two French regions.

Unlike previous studies in Scotland [12] or in the UK [11, 23], our analysis took into account all major comorbidities. Furthermore, our study is based on a robust methodology that considered the competing risk of death and of living donor transplantation to study access to the waiting list and transplantation.

After adjustment for age, all comorbidities reduced the chance of waitlisting. These findings are consistent with the few previous French studies [17, 24]. After taking into account age and the clinical characteristics, the chance of being waitlisted was 23% lower for patients in Bretagne than in Ile-de-France. Waitlisted patients had more comorbidities in Ile-de-France than in Bretagne. Moreover, mortality while on the waiting list was higher in Ile-de-France (8%) than in Bretagne (4%). These results suggest that nephrologists in Bretagne use stricter criteria than those in Ile-de-France for selecting eligible candidates for renal transplantation. During the study period, local policies of placement on transplant waiting lists (defined within each

Table 3. Association between patients' characteristics and outcomes of interest (multivariate Fine and Gray model)

	Access to waiting list for incident patients (N = 6160)			Access to transplantation ^a after placement on the list $(N = 2748)$			Access to transplantation ^a after dialysis start (N = 6160)		
	SHR	95% CI	P-value	SHR	95% CI	P-value	SHR	95% CI	P-value
Gender									
Female	1.00			1.00			1.00		
Male	1.06	1-1.2	0.144	0.96	0.9-1.1	0.495	1.07	1-1.2	0.217
Age (years)									
18–39	1.00			1.00			1.00		
40–59	0.78	0.7-0.9	<10 ⁻⁴	0.97	0.8-1.1	0.648	0.82	0.7-0.9	0.002
60–69	0.37	0.3-0.4	<10^-4	1.38	1.2-1.6	<10^4	0.57	0.5-0.7	<10^-4
70–80	0.04	0-0.1	$< 10^{-4}$	2.59	2-3.4	<10 ⁻⁴	0.08	0.1-0.1	<10^-4
Primary renal disease									
Polycystic kidney disease	1.00			1.00			1.00		
Glomerulonephritis	0.78	0.7-0.9	0.001	0.82	0.7-1	0.019	0.72	0.6-0.9	<10^-4
Hypertensive and vascular nephropathy	0.58	0.5-0.7	<10 ⁻⁴	0.87	0.7-1	0.104	0.63	0.5-0.8	$< 10^{-4}$
Diabetic nephropathy	0.53	0.4-0.7	<10 ⁻⁴	0.97	0.7-1.3	0.817	0.70	0.5-0.9	0.007
Pyelonephritis	0.72	0.6-0.9	0.005	0.78	0.6-1	0.077	0.62	0.5-0.8	0.001
Others	0.53	0.5-0.6	$< 10^{-4}$	0.76	0.6-0.9	0.001	0.53	0.4-0.6	<10^-4
First modality of dialysis									
Haemodialysis	1.00				Not signific	ant		Not signific	ant
Peritoneal dialysis	1.26	1.1-1.4	<10 ⁻⁴						
Diabetes									
No	1.00			1.00			1.00		
Yes	0.8	0.7-0.9	0.002	0.78	0.6-1	0.016	0.68	0.6-0.8	$< 10^{-4}$
Active malignancy									
No	1.00				Not signific	ant	1.00		
Yes	0.37	0.3-0.5	<10 ⁻⁴				0.34	0.2-0.5	<10^-4
Chronic respiratory disease									
No	1.00				Not signific	ant	1.00		
Yes	0.64	0.5-0.8	<10 ⁻⁴				0.52	0.4-0.7	<10^-4
Cardiovascular disease									
0	1.00			1.00			1.00		
1	0.76	0.7-0.9	<10 ⁻⁴	0.88	0.8-1	0.115	0.76	0.7-0.9	<10 ⁻⁴
2	0.58	0.5-0.7	<10 ⁻⁴	0.76	0.5-1.1	0.103	0.52	0.4-0.7	<10^4
≥3	0.51	0.4-0.6	<10 ⁻⁴	0.63	0.4-0.9	0.027	0.39	0.3-0.5	<10 ⁻⁴
Physical disabilities									
0	1.00				Not signific	ant	1.00		
≥1	0.37	0.3-0.5	$< 10^{-4}$				0.35	0.3-0.5	<10^-4
HIV infection									
No	1.00				Not signific	ant		Not signific	ant
Yes	0.6	0.5–0.7	<10^-4						
Hepatic disease									
No	1.00		_		Not signific	ant	1.00		_
Yes	0.71	0.6–0.8	<10 ⁻⁴				0.63	0.5-0.8	<10 ⁻⁴
Haemoglobin (g/dL)									
10–12	1.00				Not signific	ant		Not signific	ant
<10	0.87	0.8-1	0.004						
>12	1.02	0.9–1.2	0.76						
Emergency first dialysis session									
No		Not signific	ant		Not signific	ant		Not signific	ant
Yes									
First dialysis session with a catheter									
No	1.00				Not signific	ant	1.00		
Yes	0.78	0.7-0.9	<10 ⁻⁴				0.71	0.6-0.8	<10 ⁻⁴
TIS									
No	Available only for waitlisted		1.00		Available only for waitlisted				
Yes		patients		0.44	0.4-0.5	<10 ⁻⁴		patients	;
Blood groups									
0	Availa	ble only for	waitlisted	1.00			Availa	ble only for	waitlisted
A		patients		2.23	2–2.5	<10 ⁻⁴		patients	;
В				0.73	0.6-0.9	<10 ⁻⁴			
AB				2.76	2.1 - 3.7	<10 ⁻⁴			

Table 3. Continued

	incide	Access to waiting list for incident patients $(N = 6160)$		Access to transplantation ^a after placement on the list $(N = 2748)$			Access to transplantation ^a after dialysis start (N = 6160)		
	SHR	95% CI	P-value	SHR	95% CI	P-value	SHR	95% CI	P-value
PRA level									
<85%	Availa	Available only for waitlisted patients					Availa	ble only for	waitlisted
≥85%					0.6-0.9	0.002	patients		
Region		-						_	
Ile-de-France	1.00			1.00			1.00		
Bretagne	0.77	0.7–0.9	<10 ⁻⁴	4.52	3.8-5.4	<10 ⁻⁴	2.07	1.8-2.4	<10 ⁻⁴

HIV, human immunodeficiency virus; TIS, temporary inactive status; PRA, panel reactive antibody.

transplant centre) were implemented in France. Furthermore, with nine transplant centres in Ile-de-France and only two in Bretagne, differences in placement strategies could be accentuated. The recent recommendations of October 2015 [14] may allow better practice harmonization and limit such differences.

Our study shows that the probability of transplantation, once waitlisted, was higher for patients >60 years of age than for patients between 18 and 39 years of age. In France, the percentage of donors >65 years of age increased by a factor of 19 between 1998 and 2013 (to 37.5%) compared with the percentage of donors between 50 and 64 years of age (30%), which remained stable [18]. The higher chances of transplantation for the oldest waitlisted patients may be explained by the fact that the French allocation score favours age-matching between recipient and donor.

After adjustment for age and clinical characteristics, waitlisted patients in Bretagne were 4.5 times more likely to be transplanted than patients in Ile-de-France.

The CIF of transplantation after placement attained 50% 3.6 times earlier in Bretagne. After excluding patients with a TIS period, this delay was still longer in Ile-de-France than in Bretagne. Conversely, the rate of pre-emptive transplantation was 4% in both regions. These differences might be explained by the local organ allocation policy and the number of locally available organs, which is proportional to the number of deceased donors, which was still higher in Bretagne during the study period. In addition, organ availability was associated with transplantation after waitlisting only when the region was not included in the multivariate model. We interpreted these findings as resulting from the association between 'organ availability' and 'region' variables, of which 'region' should be considered as the main factor contributing to transplantation access (organ availability was higher in Bretagne during the study period). This limited access to renal transplantation was not attenuated by a more active policy of inclusion on the waiting list. Therefore, local strategies for promoting/limiting access to the waiting list may not influence the likelihood of receiving a successful transplantation, which remains mainly dependent on organ availability.

The percentage of patients with a TIS period, which is considered as a poor indicator of access to transplantation, has increased in France during the last 6 years [20]. Our study shows that there were more patients on TIS in Ile-de-France than in Bretagne. The median TIS duration was ~3 months longer in Ile-de-France than in Bretagne. Among pre-emptively waitlisted patients, the median TIS duration was the same in both regions, suggesting that nephrologists in these two regions have similar pre-emptive waitlisting practices.

This study has some limitations. Patients in Ile-de-France represented 82% of the entire sample. This size difference did not allow comparison of determinants of access to the waiting list and transplantation in the two regions. In addition, our analyses took into account the TIS periods, but not the reason for such TIS.

In conclusion, this study shows variations of clinical practices concerning waitlisting and TIS between nephrologists in Bretagne and Ile-de-France. More patients, and specifically more patients with comorbidities, were placed on the list in Ile-de-France than in Bretagne. Moreover, more patients had at least one TIS period in Ile-de-France than in Bretagne. However, access to renal transplantation (from the time of waitlisting or of dialysis initiation) was higher in Bretagne, where organ availability was higher during the study period. We conclude that waitlisting more patients is not sufficient to improve access to renal transplantation in the absence of a proportional increase in the number of available organs. Future work should evaluate access to transplantation after the new national recommendations for placement on the waiting list and the new national organ allocation score to harmonize practices and reduce differences between regions.

Supplementary data

Supplementary data is available online at http://ndt.oxfordjournals.org.

Acknowledgements

This work is supported by the Agence Nationale de la Recherche in the framework of the Investment for the Future program (ANR-11-IDEX-0005-02). The authors thank Dr Cécile Couchoud and Dr Christian Jacquelinet (Agence de la Biomédecine) for data extraction and for providing Supplementary data, Table S1 summarizing the French kidney allocation scheme. The authors thank also Laura Milne for English revision.

Conflict of interest statement

None declared.

References

Wolfe RA, Ashby VB, Milford EL et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. N Engl J Med 1999; 341: 1725-1730

^aDeceased donor transplantation.

- 2. Rabbat CG, Thorpe KE, Russell JD et al. Comparison of mortality risk for dialysis patients and cadaveric first renal transplant recipients in Ontario, Canada. J Am Soc Nephrol 2000;
- 3. Heldal K, Hartmann A, Grootendorst DC et al. Benefit of kidney transplantation beyond 70 years of age. Nephrol Dial Transplant 2010; 25: 1680-1687
- Franke GH, Reimer J, Philipp T et al. Aspects of quality of life through end-stage renal disease. Qual Life Res 2003; 12:
- Gentile SP, Beauger D, Speyer E et al. Factors associated with health-related quality of life in renal transplant recipients: results of a national survey in France. Health Qual Life Outcomes 2013; 11: 88
- Couchoud C, Couillerot A-L, Dantony E et al. Economic impact of a modification of the treatment trajectories of patients with end-stage renal disease. Nephrol Dial Transplant 2015;
- 7. Hauptam PJ, O'Connor KJ. Procurement and allocation of solid organs for transplantation. N Engl J Med 1997; 336: 422-431
- Satayathum S, Pisoni RL, McCullough KP et al. Kidney transplantation and wait-listing rates from the international Dialysis Outcomes and Practice Patterns Study (DOPPS). Kidney Int 2005; 68: 330-337
- Fritsche L, Vanrenterghem Y, Nordal KP et al. Practice variations in the evaluation of adult candidates for cadaveric kidney transplantation: a survey of the European Transplant Centers. Transplantation 2000; 70: 1492-1497
- 10. Stel VS, van Dijk PCW, van Manen JG et al. Prevalence of comorbidity in different European RRT populations and its effect on access to renal transplantation. Nephrol Dial Transplant 2005; 20: 2803-2811
- 11. Ravanan R, Udayaraj U, Ansell D et al. Variation between centres in access to renal transplantation in UK: longitudinal cohort study. BMJ 2010; 341: c3451
- 12. Oniscu GC, Schalkwijk AAH, Johnson RJ et al. Equity of access to renal transplant waiting list and renal transplantation in Scotland: cohort study. BMJ 2003; 327: 1261-1270

- 13. Hourmant M, De Cornelissen F, Brunet P et al. Accès à la liste d'attente et à la greffe rénale. Nephrol Ther 2013; 9: S139-S166
- 14. Transplantation rénale Accès à la liste d'attente nationale -Méthode Recommandations pour la pratique clinique. http ://www.has-sante.fr/portail/upload/docs/application/pdf/ 2015-12/rbp_recommandations_greffe_renale_vd_mel.pdf (9 March 2016, date last accessed)
- http://www.european-renal-best-practice.org/ content/ebpg-european-best-practice-guidelinesdocuments (9 October 2015, date last accessed)
- 16. Abramowicz D, Cochat P, Claas FHJ et al. European Renal Best Practice Guideline on kidney donor and recipient evaluation and perioperative care. Nephrol Dial Transplant 2014; 51: 1-8
- 17. Bayat S, Macher M, Couchoud C et al. Individual and regional factors of access to the renal transplant waiting list in France in a cohort of dialyzed patients. Am J Transplant 2015; 15: 1050-1060
- 18. Rapport annuel médical et scientifique du prélèvement et de la greffe en France. http://www.agence-biomedecine.fr/ annexes/bilan2013/donnees/sommaire-organes.htm (20 June 2016, date last accessed)
- 19. Couchoud C, Stengel B, Landais P et al. The Renal Epidemiology and Information Network (REIN): a new registry for end-stage renal disease in France. Nephrol Dial Transplant 2006; 21: 411-418
- 20. Rapport REIN 2013. http://www.agence-biomedecine.fr/Leprogramme-REIN (20 June 2016, date last accessed)
- 21. White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. Stat Med 2011; 30: 377-399
- 22. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. J Am Stat Assoc 1999; 94: 496–509
- 23. Dudley CRK, Johnson RJ, Thomas HL et al. Factors that influence access to the national renal transplant waiting list. Transplantation 2009; 88: 96-102
- 24. Bayat S, Frimat L, Thilly N et al. Medical and non-medical determinants of access to renal transplant waiting list in a French community-based network of care. Nephrol Dial Transplant 2006; 21: 2900-2907