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► **To cite this version:**

Latame Komla Adoli, Cécile Couchoud, Valérie Châtelet, Thierry Lobbedez, Florian Bayer, et al.. Lower access to kidney transplantation for women in France is not explained by comorbidities and social deprivation. *Nephrology Dialysis Transplantation*, 2024, *Nephrology, Dialysis, Transplantation: Official Publication of the European*, 39 (10), pp.1613-1623. <10.1093/ndt/gfae047>. <hal-04483609>

HAL Id: hal-04483609

<https://hal.science/hal-04483609v1>

Submitted on 24 May 2024

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Lower access to kidney transplantation for women in France is not explained by comorbidities and social deprivation

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ABSTRACT

Background. Access to kidney transplantation (KT) remains challenging for patients with end-stage kidney disease. This study assessed women's access to KT in France by considering comorbidities and neighbourhood social deprivation.

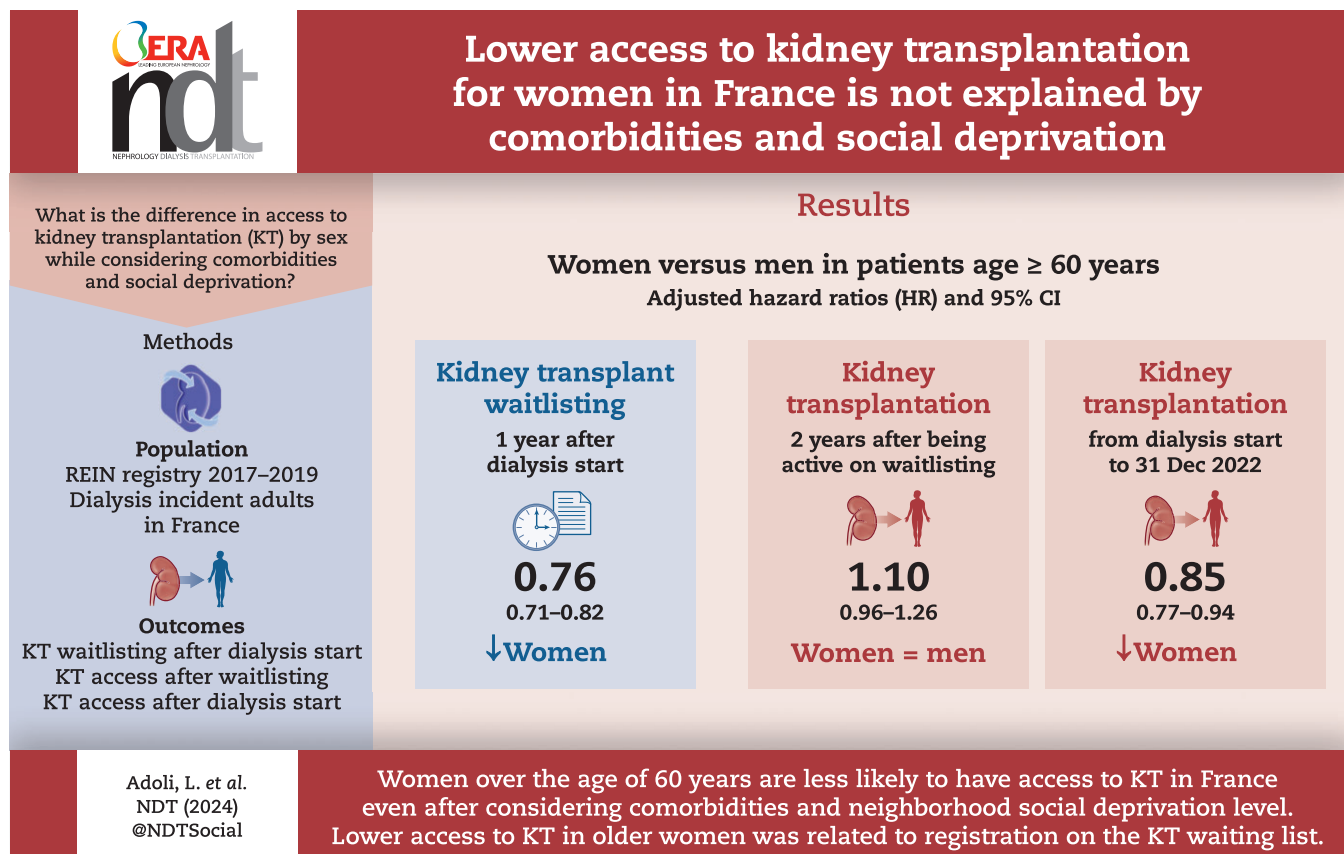
Methods. All incident patients 18–85 years old starting dialysis in France between 1 January 2017 and 31 December 2019 were included. Three outcomes were assessed: access to the KT waiting list after dialysis start, KT access after waitlisting and KT access after dialysis start. Cox and Fine–Gray models were used. Gender–European Deprivation Index and gender–age interactions were tested and analyses were performed among strata if required.

Results. A total of 29 395 patients were included (35% of women). After adjusting for social deprivation and comorbidities, women were less likely to be waitlisted at 1 year [adjusted hazard ratio [adjHR] 0.91 [95% confidence interval (CI) 0.87–0.96]] and 3 years [adjHR 0.87 (95% CI 0.84–0.91)] after dialysis initiation. This disparity concerned mainly women ≥ 60 years of age [adjHR 0.76 (95% CI 0.71–0.82) at 1 year and 0.75 (0.71–0.81) at 3 years]. Access to KT after 2 years of waitlisting was similar between genders. Access to KT was similar between genders at 3 years after dialysis start but decreased for women after 4 years [adjHR 0.93 (95% CI 0.88–0.99)] and longer [adjHR 0.90 (95% CI 0.85–0.96)] follow-up.

Conclusions. In France, women are less likely to be waitlisted and undergo KT. This is driven by the ≥ 60 -year-old group and is not explained by comorbidities or social deprivation level.

Keywords: chronic kidney disease, deprivation, gender, inequalities, kidney transplantation

GRAPHICAL ABSTRACT



KEY LEARNING POINTS

What was known:

- Kidney transplantation (KT) is the best renal replacement therapy for patients with kidney failure.
- Some medical and non-medical factors limit access to KT.
- Women are less likely to have access to KT in some French regions.

This study adds:

- Women are less likely to undergo transplantation and this is due to lower access to the waiting list.
- These gender-related disparities at the national level and in some French regions concern mainly women ≥60 years of age.
- Comorbidities and neighbourhood social deprivation did not explain these disparities.

Potential impact:

- To better understand the gender-related disparities of access to KT, studies should focus on registration on the KT waiting list.
- National and regional interventions focused on women ≥60 years of age should be developed to improve women's access to KT.

INTRODUCTION

Kidney transplantation (KT) is the best renal replacement therapy in terms of life expectancy, quality of life and economic burden [1–3] for medically eligible patients who accept this procedure. However, access to KT remains a major challenge due to an imbalance between graft supply and demand [4, 5].

In France, access to KT follows a well-defined path. First, the candidate is placed on the national kidney transplantation waiting list (KTWL) after checking for comorbidities. Once waitlisted, access to deceased donor KT is based on a national allocation score calculated by the Agence de la Biomédecine. This score takes into account the following parameters: time on dialysis; time on

the national waiting list; donor–recipient human leucocyte antigen A, B, DR and DQ mismatches; ease transplantation access indicator and donor–recipient age matching. For each pair of kidneys from a deceased donor, one is allocated locally (within the region) and the other nationally [6, 7]. Living donor recipients also need to be registered on the KTWL before undergoing KT. However, a patient on the waiting list can be on ‘temporary inactive status’ (TIS) if the initial medical check-up is not finalized or the patient’s condition does not allow performing the procedure.

Previous studies performed in various countries showed that comorbidities and different non-medical factors, such as socio-economic status, ethnicity, age or gender [8–12], limit access to the waiting list and to KT after waitlisting. Moreover, women had

lower access to KT than men [13–15]. Some studies performed in the USA concluded that socio-economic factors may explain gender-based disparities in KT access [16]. In France, results on this issue are heterogeneous. Two studies carried out in Lorraine and Bretagne, two French regions, did not show any disparity in KT access between men and women [17, 18]. However, studies including more regions found lower access for women [19, 20].

In 2015, the French national health agency [Haute Autorité de Santé (HAS)] published guidelines to harmonize practices and improve access to the KTWL and KT [21]. Since then, access to KT has not been extensively studied in France at the national and regional levels, taking into account social deprivation and comorbidities [22, 23]. The aim of this study was to assess women's access to KTWL and KT in France nationwide and in the different regions by taking into account comorbidities and social deprivation.

MATERIALS AND METHODS

Study design and population

This retrospective cohort study included all incident patients who started dialysis in France from 1 January 2017 to 31 December 2019 [21]. Patients <18 or >85 years of age were excluded.

Data collection

Data were extracted from the Renal Epidemiology and Information Network (REIN) registry [24]. Since 2012, all patients with chronic kidney disease who start a renal replacement therapy in France are recorded in this registry.

Two variable types (individual variables and a census-block deprivation index) were considered in this study. Individual variables were sociodemographic characteristics [age group, gender, occupational status (inactive: student, retired, at home, >65 years of age; active: unemployed, full-time and part-time employed), region of residence]; health-related data at dialysis initiation [primary renal disease, body mass index (kg/m²), walking impairment, number of physical disabilities, comorbidities, haemoglobin level (g/dl), albumin level (g/dl)]; and end-stage renal disease management [nephrology facility ownership, dialysis centre also performing KT, emergency first dialysis, first dialysis with catheter, autonomous first dialysis session (home, self-care unit and outpatient centre haemodialysis, non-assisted peritoneal dialysis)]. Dates of first dialysis, registration on the KTWL, KT and death were used to calculate the time at risk. For patients who initiated dialysis in a training modality, the modality used at the end of the third month was considered. For patients registered on the KTWL, additional information was collected, including TIS start and end dates, calculated panel reactive antibody (cPRA) percentage and ABO blood group.

The census block variable was the European Deprivation Index (EDI) [25, 26]. The census block is the smallest statistical unit in France and includes ≈2000 inhabitants. Each patient's address of residence was geocoded at the census block level and then the EDI was calculated. The EDI is an ecological index and a proxy of the neighbourhood socio-economic status that takes into account individual basic needs [25, 27]. These needs were defined by the European Union Statistics on Income and Living Conditions (EU-SILC) survey. EDI is a five-modality variable (from least-deprived to most-deprived quintile) calculated from general population data. The fifth quintile (Q5) represents the most-deprived areas. For this study, the EDI was coded as a binary variable (most deprived versus other).

Statistical analyses

Three outcomes of interest were considered: registration on the KTWL at 1 year (early registration) and 3 years after dialysis start, access to KT after 2 years of waitlisting and after 2 years of active status on the KTWL (for patients who were classified as TIS when waitlisted) and access to KT at 3 and 4 years after dialysis start and also considering the longest follow-up period for each patient. Only the first KT was considered in the analysis.

A cause-specific Cox proportional hazards model with death censored and a Fine-Gray model considering death, lost to follow-up and removal from the KTWL (only while studying access to KT from waitlisting time) as a competing risk for waitlisting or KT were used. Patients were followed from the follow-up start to the outcome of interest, death or the end of the follow-up period (i.e. 31 December 2022 or when they were lost to follow-up or removed from the KTWL). Patients were censored on 31 December 2022 if they did not have an outcome of interest or death. Patients were also censored when they were lost to follow-up or removed from the KTWL. For patients with a KTWL registration date identical to or earlier than the first dialysis date, time to waitlisting was set to 0.1 days after dialysis start.

All variables with a P-value <.20 in univariate analysis and all variables known to influence the outcome of interest were included in the multivariate models. A backward stepwise approach was used to extend the variable selection procedure. Missing data in our dataset were missed at random and were imputed using multiple imputation by chained equations (MICE) with five cycles [28, 29]. Gender-EDI and gender-age interactions were tested and analyses were performed among strata if required. Analyses were performed at the national and regional levels. The consistency of regional variations was assessed by quantifying the effect of heterogeneity I² [30].

Additional analyses were performed using only data for waitlisted patients on TIS. TIS frequency and duration were compared between women and men as a function of their age group. TIS at registration time and TIS after a period of active status were considered. TIS durations were compared with the Wilcoxon signed-rank test.

A P-value <.05 (two-sided) was considered significant. Only women versus men cause-specific adjusted hazard ratios (adjHRs) from Cox models were reported with their 95% confidence intervals (CIs).

Ethical considerations

Data from patients involved in this study were extracted from the French REIN registry that was approved by the Commission Nationale de l'Information et des Libertés (the French Data Protection Authority) in 2010 (agreement 903188, version 3). All patients included in the REIN registry received an information leaflet before giving their verbal consent to participate.

RESULTS

Patient's characteristics

Data from 29 395 patients (35% of women) who started dialysis in 2017–2019 were included in this study (Table 1 and Fig. 1). The median age was 68.9 years [interquartile range (IQR) 57.8–77.0] for women and 69.7 years (IQR 60.0–77.1) for men. Overall, comorbidities were more frequent in men than women at dialysis start: 49% of men and women had diabetes and 8.1% of women and 12.2% of men had an active malignancy. Moreover, 39.5% of women and 34.3% of men were in EDI quintile 5 (i.e. the most

Table 1: Baseline patient characteristics and neighbourhood social deprivation level in women and men.

Characteristics	Men	Women	Total	P-value
Patients, n (%)	19 134 (65)	10 261 (35)	29 395 (100)	
Age (years), median (IQR)	69.7 (60.0–77.1)	68.9 (57.8–77.0)	69.4 (59.2–77.1)	<.001
Age group (years), n (%)				<.001
18–39	1052 (5.5)	710 (6.9)	1762 (6.0)	
40–59	3735 (19.5)	2198 (21.4)	5933 (20.2)	
60–69	4968 (26.0)	2585 (25.2)	7553 (25.7)	
70–79	6357 (33.2)	3107 (30.3)	9464 (32.2)	
80–85	3022 (15.8)	1661 (16.2)	4683 (15.9)	
Occupational status, n (%)				<.001
Active	2076 (10.8)	906 (8.8)	2982 (10.1)	
Inactive	15 121 (79.1)	8097 (78.9)	23 218 (79.0)	
Missing	1937 (10.1)	1258 (12.3)	3195 (10.9)	
Neighbourhood deprivation level (EDI), n (%)				<.001
Most deprived	6567 (34.3)	4051 (39.5)	10 618 (36.1)	
Other	12 003 (62.7)	5891 (57.4)	17 894 (60.9)	
Missing	564 (3.0)	319 (3.1)	883 (3.0)	
Haemoglobin (g/dl), n (%)				<.001
<10	8896 (46.5)	5068 (49.4)	13 964 (47.5)	
10–12	7470 (39.1)	4008 (39.1)	11 478 (39.1)	
>12	2074 (10.8)	785 (7.6)	2859 (9.7)	
Missing	694 (3.6)	400 (3.9)	1094 (3.7)	
Albumin (g/dl), n (%)				<.001
<30	4091 (21.4)	2414 (23.5)	6505 (22.1)	
≥30	12 885 (67.3)	6656 (64.9)	19 541 (66.5)	
Missing	2158 (11.3)	1191 (11.6)	3349 (11.4)	
Body mass index (kg/m ²)				<.001
<18.5	535 (2.8)	562 (5.5)	1097 (3.7)	
18.5–23	3597 (18.8)	1939 (18.9)	5536 (18.8)	
23–25	2782 (14.5)	1043 (10.1)	3825 (13.1)	
25–30	5651 (29.5)	2352 (22.9)	8003 (27.2)	
≥30	3990 (20.9)	2848 (27.8)	6838 (23.3)	
Missing	2579 (13.5)	1517 (14.8)	4096 (13.9)	
Walking impairment, n (%)				<.001
Cannot walk	663 (3.5)	432 (4.2)	1095 (3.7)	
Walks with assistance	1608 (8.4)	1146 (11.2)	2754 (9.4)	
Autonomous	15 335 (80.1)	7817 (76.2)	23 152 (78.8)	
Missing	1528 (8.0)	866 (8.4)	2394 (8.1)	
Cardiovascular diseases, n (%)				<.001
0	8056 (42.1)	5705 (55.6)	13 761 (46.8)	
1	4037 (21.1)	2100 (20.5)	6137 (20.9)	
2	3180 (16.6)	1297 (12.6)	4477 (15.2)	
≥3	3861 (20.2)	1159 (11.3)	5020 (17.1)	
Respiratory insufficiency, n (%)				<.001
No	14 789 (77.3)	8629 (84.1)	23 418 (79.7)	
Yes	3716 (19.4)	1291 (12.6)	5007 (17.0)	
Missing	629 (3.3)	341 (3.3)	970 (3.3)	
Active malignancy, n (%)				<.001
No	16 328 (85.3)	9174 (89.4)	25 502 (86.7)	
Yes	2334 (12.2)	833 (8.1)	3167 (10.8)	
Missing	472 (2.5)	254 (2.5)	726 (2.5)	
Liver disease, n (%)				<.001
No	17 389 (90.9)	9489 (92.5)	26 878 (91.5)	
Yes	957 (5.0)	348 (3.4)	1305 (4.4)	
Missing	788 (4.1)	424 (4.1)	1212 (4.1)	
Diabetes, n (%)				.85
No	9695 (50.7)	5218 (50.9)	14 913 (50.7)	
Yes	9298 (48.6)	4981 (48.5)	14 279 (48.6)	
Missing	141 (0.7)	62 (0.6)	203 (0.7)	
Behavioural disorder, n (%)				<.001
No	17 223 (90.0)	9124 (88.9)	26 347 (89.6)	
Yes	489 (2.6)	347 (3.4)	836 (2.9)	
Missing	1422 (7.4)	790 (7.7)	2212 (7.5)	
Physical disabilities, n (%)				.02
0	17 808 (93.1)	9623 (93.8)	27 431 (93.3)	
≥1	1326 (6.9)	638 (6.2)	1964 (6.7)	
Primary kidney disease, n (%)				<.001
Diabetes	4582 (23.9)	2602 (25.3)	7184 (24.4)	
Glomerulonephritis	2226 (11.6)	952 (9.3)	3178 (10.8)	
Hypertensive and vascular disease	4934 (25.8)	2073 (20.2)	7007 (23.8)	

Table 1: Continued

Characteristics	Men	Women	Total	P-value
Other/unknown	5672 (29.6)	3423 (33.4)	9095 (30.9)	
Pyelonephritis	811 (4.3)	438 (4.3)	1249 (4.3)	
Polycystic disease	909 (4.8)	773 (7.5)	1682 (5.8)	
cPRA ^a , n (%)				<.001
0	3995 (62.2)	1459 (43.3)	5454 (55.7)	
1–24	1208 (18.8)	500 (14.8)	1708 (17.4)	
25–49	652 (10.2)	380 (11.3)	1032 (10.5)	
50–84	427 (6.7)	518 (15.3)	945 (9.7)	
≥85	136 (2.1)	515 (15.3)	651 (6.7)	
ABO blood group ^y				.47
B	2454 (38.9)	1271 (38.3)	3725 (38.7)	
AB	249 (3.94)	148 (4.5)	397 (4.1)	
B	821 (13.0)	413 (12.4)	1234 (12.8)	
O	2791 (44.2)	1490 (44.8)	4281 (44.4)	
Ownership of first dialysis facility, n (%)				.01
Private for-profit centre	5762 (30.1)	2982 (29.1)	8744 (29.7)	
Private not-for-profit centre	3017 (15.8)	1657 (16.1)	4674 (15.9)	
Public non-university hospital	5840 (30.5)	3041 (29.6)	8881 (30.2)	
Public university hospital	4488 (23.5)	2571 (25.1)	7059 (24.1)	
Missing	27 (0.1)	10 (0.1)	37 (0.1)	
Dialysis centre performing KT, n (%)				.08
No	15 983 (83.5)	8490 (82.7)	24 473 (83.3)	
Yes	3151 (16.5)	1771 (17.3)	4922 (16.7)	
Autonomous first dialysis session, n (%)				.45
No	17 973 (93.9)	9644 (94.0)	27 617 (94.0)	
Yes	1098 (5.8)	566 (5.5)	1664 (5.6)	
Missing	63 (0.3)	51 (0.5)	114 (0.4)	
Emergency dialysis start, n (%)				.08
No	13 332 (69.7)	7226 (70.4)	20 558 (70.0)	
Yes	4948 (25.8)	2552 (24.9)	7500 (25.5)	
Missing	854 (4.5)	483 (4.7)	1337 (4.5)	
First dialysis with catheter, n (%)				<.001
No	8145 (42.6)	4040 (39.4)	12 185 (41.4)	
Yes	9522 (49.8)	5376 (52.4)	14 898 (50.7)	
Missing	1467 (7.6)	845 (8.2)	2312 (7.9)	
French region, ^b n (%)				<.001
Auvergne	444 (2.3)	209 (2.0)	653 (2.2)	
Bourgogne	457 (2.4)	252 (2.5)	709 (2.4)	
Bretagne	868 (4.5)	388 (3.8)	1256 (4.3)	
Centre Val de Loire	770 (4.0)	406 (4.0)	1176 (4.0)	
Corsica	67 (0.4)	55 (0.5)	122 (0.4)	
Alsace	600 (3.1)	313 (3.1)	913 (3.1)	
Nord pas de Calais	1307 (6.8)	799 (7.8)	2106 (7.2)	
Île-de-France	3380 (17.7)	1796 (17.5)	5176 (17.6)	
Basse Normandie	385 (2.0)	219 (2.1)	604 (2.1)	
Aquitaine	976 (5.1)	451 (4.4)	1427 (4.9)	
Languedoc Roussillon	889 (4.6)	451 (4.4)	1340 (4.6)	
Pays de la Loire	867 (4.5)	434 (4.2)	1301 (4.4)	
Provence Alpes Côte Azur	1643 (8.6)	791 (7.7)	2434 (8.3)	
Guadeloupe	132 (0.7)	96 (0.9)	228 (0.8)	
Martinique	153 (0.8)	109 (1.1)	262 (0.9)	
French Guiana	99 (0.5)	62 (0.6)	161 (0.5)	
Réunion	392 (2.0)	346 (3.4)	738 (2.5)	
Mayotte	55 (0.3)	34 (0.3)	89 (0.3)	
Rhône-Alpes	1632 (8.5)	891 (8.7)	2523 (8.6)	
Franche-Comté	297 (1.6)	164 (1.6)	461 (1.6)	
Champagne-Ardenne	397 (2.1)	230 (2.2)	627 (2.1)	
Lorraine	796 (4.2)	443 (4.3)	1239 (4.2)	
Picardie	542 (2.8)	324 (3.2)	866 (2.9)	
Haute-Normandie	538 (2.8)	304 (3.0)	842 (2.9)	
Limousin	218 (1.1)	99 (1.0)	317 (1.1)	
Poitou-Charentes	412 (2.2)	190 (1.9)	602 (2.0)	
Midi Pyrénées	818 (4.3)	405 (3.9)	1223 (4.2)	

^aCollected mainly for patients registered on the KTWL.^bFrench regions based on the region organization before 2015.

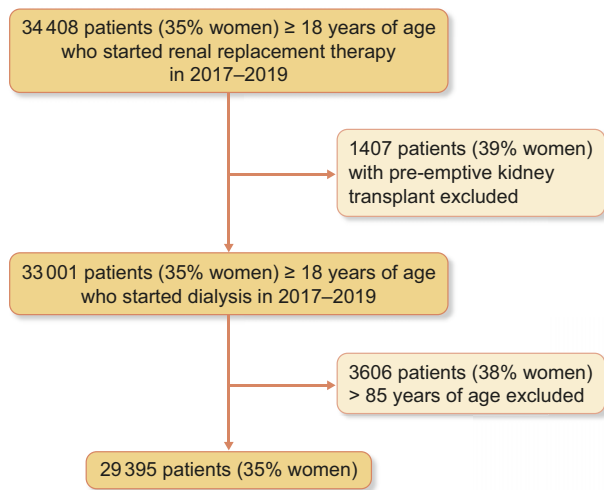


Figure 1: Study flow diagram presenting patients selection.

disadvantaged level) (Table 1 and Fig. 2). Death was more frequent among men than women after dialysis start and after registration on the KTWL (Table 2).

Access to the KTWL at 1 and 3 years after dialysis start

At 1 and 3 years after dialysis initiation, 24% (24% of men and 24% of women) and 33% of patients (33% of men and 32% of women) were registered on the KTWL, respectively. At both time points, the death rate was higher in men (Table 2). One year after dialysis initiation, women were less likely to be registered on the KTWL than men after adjusting for comorbidities and EDI [adjHR 0.91 (95% CI 0.87–0.96)]. There was a significant gender–age interaction [adjHR gender × age: 0.76 (95% CI 0.68–0.84)], therefore analyses were performed among age strata. The stratification cut-off point was chosen on the basis of changes in the HR across age groups (Supplementary Fig. S1). The age-stratified analysis did not find any gender-related difference in KTWL access in patients <60 years of age [adjHR 1.03 (95% CI 0.96–1.10)]. Conversely, women ≥60 years of age were less likely to be waitlisted compared with men [adjHR 0.76 (95% CI 0.71–0.82)]. Similar results were obtained at 3 years after dialysis start. Overall, women had less access to the KTWL than men [adjHR 0.87 (95% CI 0.84–0.91)]. In the stratified analysis, no between-gender difference was observed in patients <60 years of age [adjHR 0.99 (95% CI 0.94–1.05)], but was seen in patients ≥60 years of age [adjHR 0.75 (95% CI 0.71–0.81)] (Fig. 3). There was no gender–EDI interaction for access to the KTWL at 1 year [adjHR 0.99 (95% CI 0.90–1.11)] and 3 years [adjHR 1.00 (95% CI 0.91–1.09)]. At the regional level, the same analyses showed that women were less likely to have access to the KTWL at 1 year after dialysis start in three regions: Aquitaine [adjHR 0.79 (95% CI 0.63–0.99)], Languedoc Roussillon [adjHR 0.72 (95% CI 0.55–0.95)] and Pays de Loire [adjHR 0.78 (95% CI 0.62–0.98)]. At 3 years after dialysis start, access was still lower in these three regions and also in Bourgogne [adjHR 0.62 (95% CI 0.46–0.86)] and Île-de-France [adjHR 0.90 (95% CI 0.82–0.98)] (Fig. 4 and Supplementary Tables S1 and S2).

Access to KT after registration on the waiting list

At 2 years after registration on the KTWL, 35% of men and 39% of women underwent KT. When only patients with active sta-

tus on the KTWL were considered, the percentages increased to 41% for men and 43% for women. The death rate was higher among men than women (Table 2). No difference between men and women was found regarding access to KT at 2 years after registration on the KTWL [adjHR 1.01 (95% CI 0.94–1.10)] and after 2 years of active status on the KTWL [adjHR 0.97 (95% CI 0.90–1.05)]. The age-stratified analysis showed that in patients <60 years of age, access to KT was similar between genders after 2 years of registration (any status) [adjHR 0.95 (95% CI 0.87–1.05)] and after 2 years of active status on the KTWL [adjHR 0.92 (95% CI 0.83–1.01)]. In patients ≥60 years of age, women were more likely to have access to KT than men after registration on the KTWL (any status) [adjHR 1.16 (95% CI 1.01–1.33)]. No between-gender difference was observed in patients ≥60 years of age after 2 years of active status [adjHR 1.10 (95% CI 0.96–1.26)] (Fig. 3).

At the regional level, in Haute Normandie, women were less likely to have access to KT after 2 years of registration on the KTWL (any status) compared with men [adjHR 0.56 (95% CI 0.34–0.92)]. Conversely, they were more likely to undergo KT in Bourgogne [adjHR 3.48 (95% CI 1.68–7.20)] and Franche-Comté [adjHR 2.78 (95% CI 1.18–6.54)]. After 2 years of active status on the KTWL, women were still more likely to undergo KT in Bourgogne [adjHR 3.20 (95% CI 1.64–6.26)], whereas they were less likely in Île-de-France [adjHR 0.81 (95% CI 0.67–0.98)] and Limousin [adjHR 0.14 (95% CI 0.02–0.94)]. No significant difference was found in the other regions (Supplementary Tables S3 and S4).

Access to KT since dialysis start

Three years after dialysis start, 12% of men and 14% of women underwent KT (Table 2). The analyses performed in all incident patients [adjHR 0.98 (95% CI 0.92–1.05)] and in patients <60 years of age [adjHR 0.99 (95% CI 0.91–1.08)] and ≥60 years of age [adjHR 0.97 (95% CI 0.86–1.09)] did not find any difference between women and men in access to KT after dialysis initiation (Fig. 3).

At 4 years after dialysis start, overall (all patients and nationwide), women were less likely to have undergone KT [adjHR 0.93 (95% CI 0.88–0.99)]. The age-stratified analysis did not find any difference between genders.

In patients with longer follow-up, women had lower access to KT than men [adjHR 0.90 (95% CI 0.85–0.96)], but this was driven by the older age group [≥60 years; adjHR 0.85 (0.77–0.94)]. Additional results on KT access in the different French regions can be found in Supplementary Table S5.

The Fine–Gray model produced results similar to those of the Cox models (results at the national level are in Supplementary Table S6; the cumulative incidence functions are in Supplementary Figs. S2–S4).

Analysis of patients with pre-emptive KT

In 2017–2019, 1407 patients received a pre-emptive KT and were not included in the previously described analyses. Their mean age was 52 years (standard deviation 5) and 39% were women. Additional results on this group are provided in Supplementary Table S7.

Analysis of patients on TIS

During the study period, 10 030 patients (34% of incident dialysis patients) were registered on the KTWL. Among them, 67% were classified as TIS upon waitlisting (67% of women and 66%

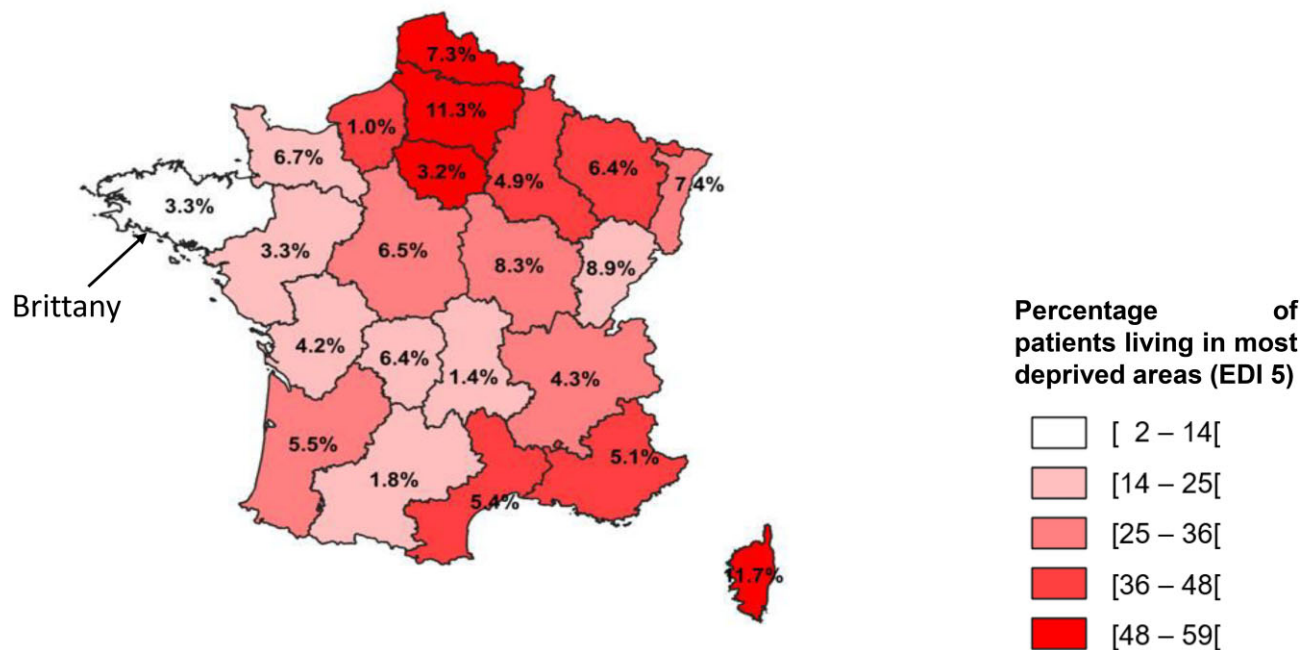


Figure 2: Percentage of patients living in the most deprived areas (EDI 5) and difference between genders per region in France (e.g. in Brittany, 2–14% of patients lived in the most deprived areas; the percentage of women living in the most deprived areas was 3.3% higher than in men).

Table 2: Description of the outcomes according to the follow-up duration and the patients' gender.

Access	Total follow-up duration (years)	Mean follow-up duration (days)	Outcomes	Men, n (%)	Women, n (%)	Total, N (%)	P-value
Access to KTWL from dialysis start	1	273	Registration on the list	4548 (24)	2451 (24)	6999 (24)	.82
			Death	2677 (14)	1179 (11)	3856 (13)	<.01
	3	629	Registration on the list	6327 (33)	3325 (32)	9652 (33)	.25
			Death	5725 (30)	2641 (26)	8366 (28)	<.01
Access to KT from registration on KTWL	2	560	Transplantation	2110 (35)	1216 (39)	3326 (36)	<.01
			Death	306 (5)	115 (4)	421 (5)	<.01
Access to KT from active registration on KTWL ^a	2	502	Transplantation	2197 (41)	1243 (43)	3440 (42)	.04
			Death	319 (6)	125 (4)	444 (5)	<.01
Access to KT from dialysis start	3	829	Transplantation	2371 (12)	1403 (14)	3774 (13)	<.01
			Death	6086 (32)	2774 (27)	8860 (30)	<.01
	4	1069	Transplantation	2913 (15)	1645 (16)	4558 (15)	.25
			Death	7092 (37)	3349 (33)	10 441 (35)	<.01
Full follow-up period		1079	Transplantation	3273 (17)	1818 (18)	5091 (17)	.19
			Death	7959 (42)	3771 (37)	11 730 (40)	<.01

^aActive registration is from when the patient is no longer on TIS.

of men). The median TIS duration was similar between genders: 168 days (IQR 76–374) for men and 168 days (IQR 71–373) for women. TIS duration was shorter for patients <60 years of age [164 days (IQR 70–373) for women and 162 days (IQR 77–353) for men] than for patients ≥60 years of age [172 days (IQR 73–394) for women and 172 (IQR 75–399) for men]. After an active status period on the KTWL, time before the first TIS was similar between men and women in both age groups ($P = .43$). However, men ≥60 years of age spent more time as TIS [112 days (IQR 49–228)] than women [96 days (IQR 45–213)] (Supplementary Tables S8 and S9).

DISCUSSION

This is the first study on gender-related disparities of access to KT in France at the national and regional levels that took into account the patients' characteristics and also the neighbourhood social deprivation (EDI). This study found that overall, women were less likely to have access to KT in France even after controlling for all comorbidities and EDI at the census block level and after considering death, loss to follow-up and removal from the waiting list as competing risks to registration on the KTWL/KT. These disparities were driven mainly by women ≥60 years of age and were observed in several French regions. Indeed, lower access to KT was due to

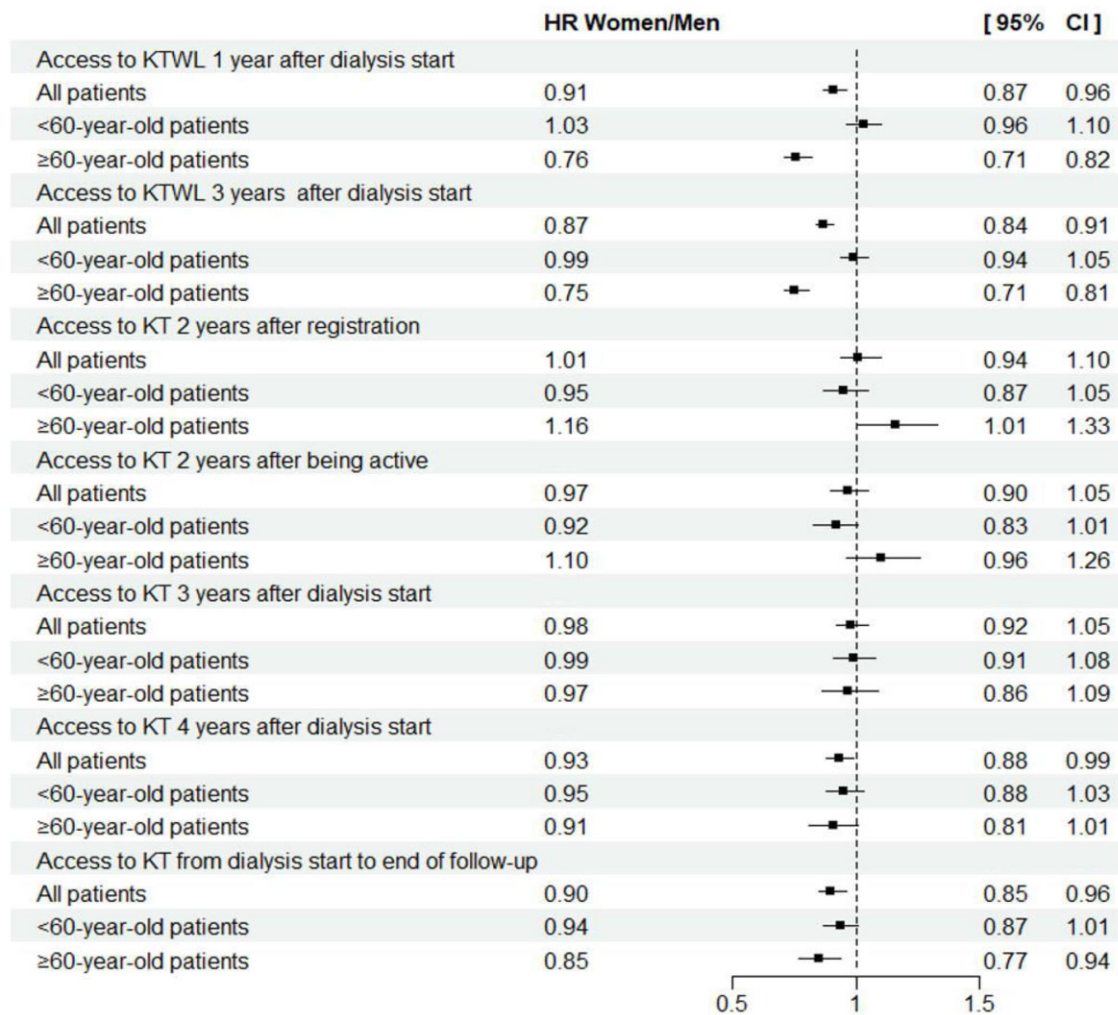


Figure 3: Association between gender and access to KTWL or KT (multivariable Cox model with death censored). All models were adjusted for baseline comorbidities and EDI level. The figure shows the HRs and 95% CIs of women versus men for the whole cohort and for the age-stratified analyses.

disparities in registration on the KTWL; after being registered, no difference in access to KT was observed between men and women.

Compared with men, women were 9% and 13% less likely to be registered on the KTWL at 1 and 3 years, respectively, after dialysis start; in particular, patients ≥ 60 years of age. Similar results were obtained in Austria [31] and in some other European countries [14, 32]. In the USA, a study reported that women were 11% less likely to be waitlisted [33]. In Canada, women were 12% less likely to be referred for KT compared with men [34]. A study performed in France in 2012 found that women were 11% less likely to be registered on the KTWL after a median follow-up period of 8 months after dialysis start [20]. However, these studies did not take into account the neighbourhood deprivation level and an exhaustive list of comorbidities. In 2015, the French HAS published national recommendations to harmonize practices and reduce disparities in access to the KTWL [21]. Our results show that several years after their publication, disparities still exist, particularly in women ≥ 60 years of age. In the USA, some studies suggested that patient choice could explain this disparity and that women are more likely to refuse referral for KT [20, 35]. Therefore, we are now conducting a qualitative study to understand the reasons underlying patients' choices [36].

Our study showed that after being registered on the KTWL, there was no difference in access to KT between genders [adjHR

1.01 (95% CI 0.94–1.10)]. A study performed on incident dialysis patients in France reported similar results [10]. Conversely, in a USA study, women were 4% less likely to access deceased donor KT after waitlisting [33]. Some studies suggested that the high cPRA level in women, mainly due to previous pregnancies, is associated with lower access to KT [35, 37]. In the present analysis, the cPRA level was taken into account, considering both living and deceased donors, and no gender-based difference in access to KT was observed after waitlisting. Moreover, graft allocation in France is based on a national score calculated by the Agence de la Biomédecine that does not take into account the recipients' gender [7]. These facts could partly explain the difference between our study and USA studies. The age-stratified analyses did not find any difference between women and men after 2 years of active status on the KTWL. However, women ≥ 60 years of age were 16% more likely to have access to KT after 2 years of waitlisting. This result could be due to the fact that in our study, older men had more comorbidities than women and therefore they were more likely to be placed on TIS than women once registered. In agreement, men ≥ 60 years of age spent more time on TIS than women ≥ 60 years of age.

Analysis of access to KT from dialysis start showed that women, particularly those ≥ 60 years of age, were less likely to undergo KT, in agreement with previous studies [38–40]. This

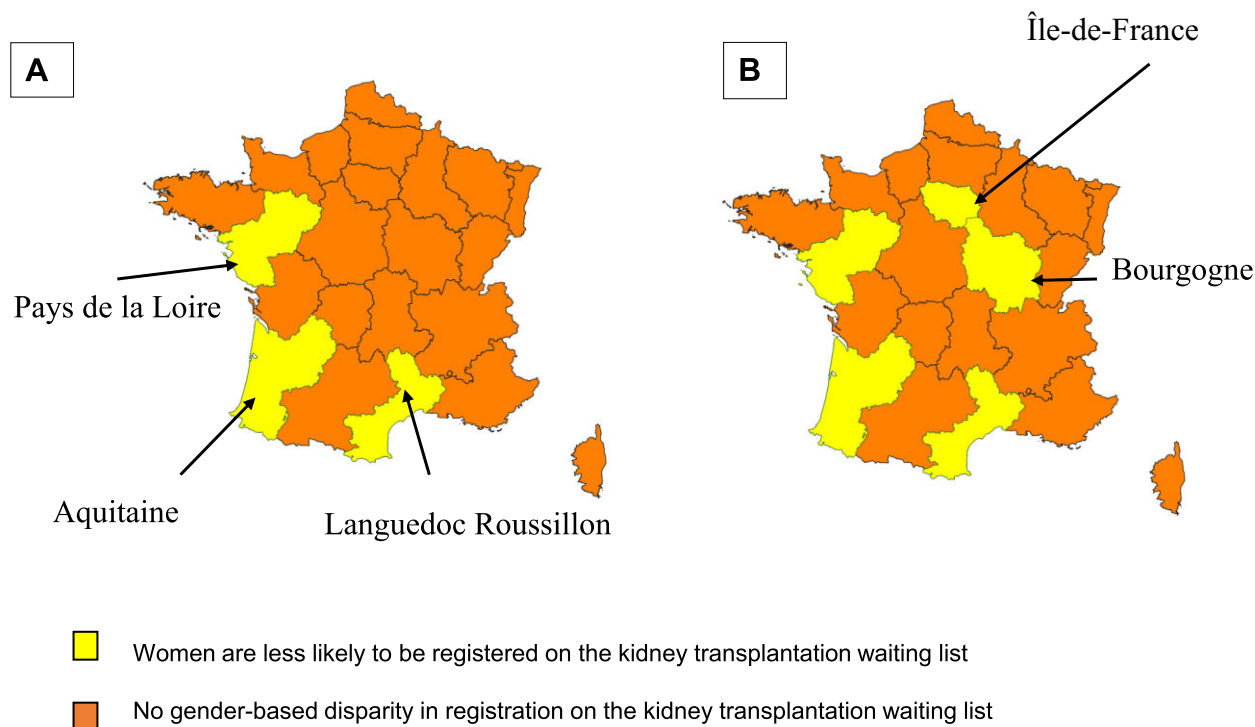


Figure 4: Map showing access to the KTWL in regions at (A) 1 year and (B) 3 years after dialysis start. Overseas regions are not represented.

was a consequence of the lower access to registration on the KTWL. Gender-based disparities have been extensively described. In 1988, in the USA, Kjellstrand showed that women and older patients had less access to KT than men and younger patients [41]. Older women may have a different perception of their disease and different perspectives that influence their views on KT [42]. Several studies have tried to explain these gender-based disparities. In the USA, women are less likely to be referred to a transplantation centre [43–45]. Some authors argue that this disparity is due to faster disease progression in men than women [46, 47]. However, other authors have shown that it is mainly due to lower information about KT provided to women [48] and the fact that women are more likely to refuse KT [20]. A novel education approach [49] that focuses particularly on older women could help to change their perspectives on KT.

The present analysis highlighted similar gender-related disparities of access to the KTWL and KT in several French regions (Supplementary Tables S1–S5). Access to the KTWL and KT were not homogeneous in France and varied among regions. Like at the national level, these disparities were not related to comorbidities, social deprivation level (EDI) or the availability of transplantation activity at the patient dialysis centre, as the analyses were adjusted for these factors. However, several factors may explain these disparities among French regions. One could be the practices of nephrologists concerning registration on the KTWL, temporary contraindications and the timeline of the pre-KT medical check-up, which are not the same in all regions. In addition, KT refusal by patients may not be heterogeneous across French regions. A qualitative study is currently being carried out to clarify these points.

In our study, no gender–EDI interaction was observed. After adjusting for the EDI level, women still had less access to the KTWL. Most previous studies performed in France on KT and KTWL ac-

cess did not control for social deprivation [10, 17, 20]. Some of the studies that took into account social deprivation level were less likely to be on self-care dialysis [50]. In a Canadian study, the median neighbourhood income was not associated with patient referral for KT and women still had lower access to the first step of the KT path [34].

The size of the study population was the main strength of this study. Moreover, access to KT was studied throughout its various steps and gender-based disparities were exhaustively and precisely assessed at the French national and regional levels. Similar results were obtained with the Cox and Fine–Gray models.

Our study has some limitations. Access to KT was studied at 3 years after dialysis initiation. Three years of follow-up can be short to precisely assess disparities in KT. However, an additional analysis was performed using the maximum follow-up duration for each patient and the results reinforced our findings. As the REIN registry does not include information on the patients' socioeconomic status, analyses were adjusted for the neighbourhood EDI. However, EDI is an ecological variable coded at the census block level and may not reflect the real individual economic status. Lastly, although our models took into account many confounders selected using different variable selection approaches, other variables not collected in the REIN registry could have influenced the results.

In conclusion, this study clearly shows that women ≥ 60 years of age are less likely to have access to KT in France, even after considering all comorbidities and the neighbourhood social deprivation level. This lower access was related to the step of registration on the KTWL and was also observed in some regions. Social deprivation and comorbidities did not explain the women's lower access to KT in France. A qualitative study is ongoing to better understand how the patients' perspectives and nephrologists' practices might explain these gender-related disparities.

SUPPLEMENTARY DATA

Supplementary data are available at [ndt](#) online.

ACKNOWLEDGEMENTS

The authors thank Elisabetta Andermarcher for English revision.

FUNDING

This research was funded in whole by the French National Research Agency (ANR-20-CE36-0002-01). The funding source had no role in the study.

AUTHORS' CONTRIBUTIONS

A.L.K., B.S., J.J.P. and C.C. were responsible for the methodology. B.S. was responsible for project administration. A.L.K. and B.S. wrote the original draft. All authors were responsible for the conceptualization and review and editing of the manuscript. All authors have read and agreed to the submitted version of the manuscript.

DATA AVAILABILITY STATEMENT

Access to national data is regulated by an Agence de la Biomédecine scientific committee that analyses each request. In this context, data are available upon request. If readers need information about REIN registry data, they can contact C.C. (cecile.couchoud@biomedecine.fr), who coordinates the REIN at the national level.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to disclose.

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