ORIGINAL ARTICLE

Renal transplantation outcome and social deprivation in the French healthcare system: a cohort study using the European Deprivation Index

Valérie Châtelet[1], Sahar Bayat-Makoei[2], Cécile Vigneau[3], Guy Launoy[4] & Thierry Lobbedez[1]

1 Centre Universitaire des Maladies Rénales, CHU de Caen, Caen Cedex 9, France
2 EHESP Rennes, Sorbonne Paris Cité, EA 7449 REPERES, Rennes, France
3 Service de Néphrologie, CHU Pontchaillou, Rennes, France
4 Centre de Lutte Contre le Cancer François Baclesse, U1086 Inserm, 'ANTICIPE', Caen Cedex 05, France

Correspondence
Thierry Lobbedez, 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: lobbedez-t@chu-caen.fr

SUMMARY

The study objective was to estimate the effect of social deprivation estimated by the European Deprivation Index (EDI) on the risk of death and graft failure on renal transplantation in France. EDI was calculated for 8701 of 9205 patients receiving a first renal transplantation between 2010 and 2014. Patients were separated in EDI quintiles of the general population. A Cox model (cs-HR: cause-specific hazard ratio of death or graft failure) and a Fine and Gray model (sd-HR: subdistribution hazard ratio of death and graft failure) were used for the analysis. The 5th quintile group (most deprived) accounted for 32% of patients [2818 of 8701]. In the multivariate analysis, compared with quintile 1, the risk of death was higher for the 5th quintile group in the complete cohort [cs-HR: 1.31, 95% CI: (1.01–1.70), sd-HR: 1.29, 95% CI: (1.00–1.68)], in the deceased donor group [cs-HR: 1.31, 95% CI: (1.00–1.71), sd-HR: 1.30, 95% CI: (1.00–1.70)] but not in living donor transplant patients. There was no association between the EDI groups and the risk of transplant failure. Social deprivation estimated by the EDI is associated with an increased risk of death in transplantation in France but not with the chance of allograft loss.

Transplant International 2018; 31: 1089–1098

Key words
European Deprivation Index, outcome, renal transplantation, social deprivation, socio-economic inequalities

Received: 24 November 2017; Revision requested: 15 January 2018; Accepted: 22 March 2018; Published online: 16 April 2018

Introduction

Social inequalities in health (SIH) are one of the consequences of social deprivation, a broad and multidimensional concept referring to social position defined according to a social gradient and having an impact on health status [1]. One of the objectives of health policies is to reduce SIH and thereby improve the health status of the population, regardless of the social status of individuals. In Europe, the organization of health systems is country-specific so indicators specific to each nation have been developed to measure social deprivation and estimate the effectiveness of health policies [2]. Comparing the effect of health policies in European countries on reducing social inequalities in health requires a common measure of social deprivation. The European Deprivation Index (EDI) is a transnational European ecological index of social deprivation based on a European study [3,4]. It has been demonstrated that EDI is a proxy of individual socio-economic status [5]. In France, the EDI is associated with cancer incidence [6]. It is grounded on the assumption that the experience of

doi:10.1111/tri.13161

social deprivation, which is based on the concept of the satisfaction of basic needs, is shared by the inhabitants of each European country. The EDI relies on the concept of perceived fundamental needs or necessities of life. This conceptual definition of deprivation is based on the population's own perception of poverty. The EDI allows comparison between nations as the same concept is used to measure social deprivation in different countries.

In both the United States and the United Kingdom, it has been demonstrated that social inequalities in health have an impact on the access to renal transplantation, on transplant survival and on the mortality of transplanted patients [7–9]. The effect of social deprivation on the outcome of transplanted patients is likely to depend on the organization of national health systems and health policies. The EDI would enable comparative studies in renal transplantation to be carried out between different European countries. To our knowledge, no study to date has assessed the impact of social deprivation on renal transplantation outcomes using a transnational indicator. There is no study about the effect of social deprivation on the outcome of renal transplantation at the national level in France [10]. One of the aims of our study was to estimate the exposure to social deprivation, as estimated by the EDI, in patients who received a first renal transplant in France. The main objective of the study was to investigate the prognostic value of the EDI, and its association with transplant failure or mortality [11].

Patients and methods

Study population

This was a retrospective study using data from the Cristal database of the French agency (Agence de la Biomédecine) where the data of transplanted patients in the 32 French transplantation centres are registered. In France, transplantation centres must enter patient information in the database at registration on the waiting list, at the time of transplantation and to provide follow-up when death or transplantation failure occurs. Patients older than 18 years receiving a first renal transplantation from a living or a deceased donor in France between 1st January 2010 and 31st December 2014 were included in the study. We excluded patients receiving multiorgan transplantation and those with a liver or cardiac transplant. The end of the observation period was 1 June 2016. There were 9205 transplanted patients in the original data set. Of these 9205 patients, there were 8701 patients who had a precise home address (required for the EDI calculation), registered in the database at the time of registration on the waiting list and who formed the final data set.

Events of interest

We examined the time to occurrence of two events during transplantation: death and transplantation failure. Death and transplantation failure were competing events. Transplantation failure was defined as a permanent return to dialysis or a second transplantation. Survival time was defined as the time from renal transplantation until death (transplantation failure censored) or until transplantation failure (death-censored) or the end of follow-up.

Definition of covariates

European Deprivation Index

The explanatory variable was the EDI estimated with the patient's home address at registration on the waiting list. Each transplanted patient was attributed the smallest geographical unit that corresponded to his home address. The smallest geographical unit, which corresponded to 2000 inhabitants (IRIS: regrouped statistical block), was provided by the National Institute for Statistics and Economic Studies (INSEE). The EDI was calculated for each IRIS, and then patients were separated into five groups based on the EDI quintiles determined in the French population [3]. The assessment of individual socio-economic status at IRIS level ensures the homogeneity of the socio-economic characteristics of individuals and limits the ecological bias. The EDI is a proxy of the deprivation of individuals as it is constructed from covariates obtained at individual level from an EU-SILC annual European survey. Objective poverty was defined as a standard of living below 60% of the media standard of living among the whole national population. Subjective poverty was defined by questions of the EU-SILC survey. Six fundamental needs associated with both objective and subjective poverty were selected by multivariate logistic regression. Individuals were defined as deprived if they could not afford at least three fundamental needs. Thereafter, variables available both in the EU-SILC and at the IRIS level were selected. The regression coefficients of these variables associated with poverty were obtained by logistic regression. These coefficients became the weights of the rate of the fundamental needs at the IRIS level. The score of the EDI was subsequently calculated for each IRIS and

Transplant International 2018; 31: 1089–1098

validated with the degree between of its association with income and education, and the Townsend score (3). It has been demonstrated that the EDI was an accurate proxy for individual deprivation (5).

Patient characteristics

The following patient characteristics at registration on the waiting list were extracted from the Cristal database: age at transplantation, gender, 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 haemodialysis), hepatitis C virus infection (HCV), pre-emptive registration and pre-emptive transplantation. Pre-transplant dialysis duration was divided into tertiles, and a category was added for pre-emptive transplant patients.

Transplantation characteristics

Donor source was classified as either living or deceased donor. Donor age, gender and BMI were obtained from the database. The number of human leucocyte antigen (HLA) mismatches between the donor and the recipient was calculated and divided into three categories. Cold ischaemia time, donor comorbidities (hypertension, diabetes), donor cause of death (cardiovascular) and the estimated glomerular filtration rate (MDRD) were extracted from the registry for the subgroup of deceased-transplanted patients. Delayed graft function was defined by a serum creatinine level above 2.8 mg/dl.

Statistical analysis

Statistical analysis was performed separately on the complete cohort, on the deceased donor and on the living donor subgroup. For univariable analysis, transplanted patients were described according to the five groups of the EDI (called EDI quintiles for clarity) (Table 1). The categorical covariates were expressed as frequencies and percentages, and the continuous covariates were expressed as the median with the first and third quartiles. To avoid multiple testing issues, no statistical test was performed for group description.

The association between individual characteristics at registration and the quintile 5 of the EDI (most deprived status) was assessed by a bivariable and a multivariable log-binomial regression model. Covariates were selected for the multivariable analysis if the *P* value was below 0.20 in the bivariable analysis. As diabetic nephropathy could mask the association of diabetes *per se* with quintile 5 of the EDI, two separate models with and without underlying nephropathy were built. Confidence intervals (95% CI) were used to represent the uncertainty of the relative risk (RR).

To explore the relationship between each covariate and each event of interest in an aetiological approach, we estimated the unadjusted cause-specific hazard ratio (cs-HR) with a Cox regression model. We also draw cumulative incidence function curves for each outcome (quintile 5 versus other quintiles). For the prognostic evaluation of the effect of covariates on the outcome, a bivariable analysis was performed with the Fine and Gray regression model, which allows the subdistribution hazard ratio (sd-HR) to be estimated. Regression splines were used to explore the functional form of the continuous variables. Proportionally, assumptions were tested with visual inspection of the Schoenfeld residual plots. Outliers were detected with DfBeta plots. Confidence intervals (95% CI) were used to represent the uncertainty of the HRs. Collinearity between covariates was tested with the variance-inflated factor.

The EDI quintiles groups were entered in the multivariable analysis *a priori* without undertaking any statistical procedure. The association between social deprivation and outcome was assessed with the EDI quintiles classified in categories (quintile 1 as reference level) and with the EDI quintile as an ordinal covariate (*P* trend from quintile 1 to quintile 5). Covariates were otherwise included in the multivariable analysis if the *P* value was <0.20 in the bivariate analysis. We only tested the interaction between EDI and age, gender and diabetes.

Missing data

The rate of missing data was lower than 15% for each covariate of the data set; a multiple imputation by chained equation was performed for all missing data. All statistical analyses were performed with R 3.1.2. (R Foundation for Statistical Computing).

The study received the approval of the West of France Ethics Committee (reference number A15-D18-VOL.25).

Results

Characteristics of patients

The median follow-up time was 48.82 months. Among the patients included in the analysis, 2818 patients were in the quintile 5 group, that is 32.4% of the study population [quintile 1: 1272 of 8701 (14.6%), quintile 2:

Table 1. Patient characteristics (complete cohort).

N = 8701	Quintile 1 (*N* = 1272)	Quintile 2 (*N* = 1391)	Quintile 3 (*N* = 1524)	Quintile 4 (*N* = 1696)	Quintile 5 (*N* = 2818)
Age [median (IQR)]	57 [47–65]	55 [46–65]	57 [45–65]	56 [45–65]	54 [43–63]
Gender (male)	66% (838)	66% (921)	65% (990)	64% (1088)	61% (1714)
BMI (kg/m^2)					
<20	3% (36)	3% (35)	3% (46)	3% (49)	3% (81)
[20–25]	50% (638)	49% (675)	47 (719)	50% (854)	47% (1317)
>25	47% (598)	49% (681)	50% (759)	47% (793)	50% (1420)
Foreign-born	16% (209)	17% (243)	21% (327)	27% (453)	49% (1367)
Underlying nephropathy					
Diabetic	8% (100)	9% (120)	9% (138)	10% (169)	13% (368)
Glomerulonephritis	24% (309)	25% (352)	24% (368)	24% (401)	19% (549)
Interstitial nephritis	8% (102)	9% (128)	9% (144)	9% (152)	9% (263)
PKD	23% (289)	23% (324)	21% (320)	20% (334)	14% (383)
Systemic disease	3% (43)	3% (48)	4% (60)	3% (59)	3% (92)
Uropathy	2% (29)	3% (37)	2% (36)	3% (47)	2% (55)
Vascular	10% (133)	8% (116)	9% (132)	9% (149)	12% (336)
Miscellaneous	6% (73)	5% (64)	5% (80)	5% (87)	6% (173)
Unknown	15% (194)	15% (202)	16% (246)	18% (298)	21% (599)
Diabetes	15% (190)	16% (228)	15% (228)	16% (266)	20% (554)
Cardiovascular disease	24% (301)	24% (328)	24% (368)	22% (379)	24% (665)
Tobacco					
Non-smoker	52% (661)	52% (719)	52% (797)	50% (853)	52% (1467)
Smoker	16% (208)	17% (241)	18% (267)	20% (340)	20% (570)
Former smoker	32% (403)	31% (431)	30% (460)	30% (503)	28% (781)
Hypertension	69% (882)	68% (952)	68% (1036)	67% (1131)	69% (1947)
Chronic pulmonary disease	2% (28)	3% (37)	3% (45)	2% (41)	2% (69)
Liver cirrhosis	1% (9)	1% (16)	1% (17)	1% (16)	1% (25)
Pre-emptive registration	42% (532)	39% (547)	38% (573)	34% (584)	28% (790)
Pre-emptive transplantation	20% (252)	19% (268)	17% (264)	17% (283)	12% (330)
Peritoneal dialysis	16% (157)	14% (157)	14% (176)	14% (189)	10% (242)
Dialysis duration (months)					
Pre-emptive	19% (252)	19% (268)	17% (264)	16% (283)	11% (330)
Tertile 1 [0.03–18.50]	32% (406)	32% (441)	32% (481)	27% (455)	23% (630)
Tertile 2 [18.50–37.40]	26% (322)	26% (367)	28% (429)	31% (518)	27% (769)
Tertile 3 [37.40–395.00]	23% (292)	23% (315)	23% (350)	26% (440)	39% (1089)
Donor source (living donor)	16% (209)	16% (220)	14% (219)	15% (251)	12% (326)

1391 of 8701 (16%), quintile 3: 1524 of 8701 (17.5%) and quintile 4: 1696 of 8701 (19.5%)]. The average age was similar between the five quintiles groups, and there was a majority of men in each quintile [quintile 1: 838 (66%), quintile 2: 921 (66%), quintile 3: 990 (65%), quintile 4: 1088 (64%) and quintile 5: 1714 (61%)]. The most frequent nephropathy observed was glomerular nephropathy, the proportion of diabetic nephropathy being higher for quintile 5 patients (13% vs. 8% for the 1st quintile). Among patients of the quintile 5 group, 20% were diabetic compared with 16% of patients of the quintile 4 group, 15% in quintiles 1 and 3 and 16% in quintile 2. Patients in quintile 5 were more likely to be foreign-born than in the other quintiles (quintile 5: 49% vs. quintile 1: 16%, quintile 2: 17%, quintile 3: 21%, quintile 4: 27%).

Pre-emptive registrations accounted for 42% of patients in quintile 1 vs. 28% for patients in quintile 5. Thus, the proportion of patients who received a pre-emptive transplant was 20% in quintile 1 vs. 12% in quintile 5. Patients in quintile 5 had a longer duration of dialysis than those in the other quintiles (Table 1). In the multivariable analysis, the demographic characteristics of patients associated with quintile 5 were age under 60 years [RR: 1.28, 95% CI: (1.20–1.37)], female gender [RR: 1.30, 95% CI: (1.20–1.45)] and hepatitis C [RR: 1.35, 95% CI: (1.16–1.55)].

EDI and risk of death

Among the 8701 subjects, there were 610 deaths (cumulative probability of the event of interest: 6.76%). Cumulative incidence curve of death is displayed in Fig. 1. In multivariable analysis with the Cox model, taking quintile 1 as a reference class and adjusting for the variables selected in the bivariable analysis, the risk of death among renal transplant patients was higher for patients of the quintile 5 in the complete cohort [cs-HR: 1.31, 95% CI: (1.01–1.70)] and in patients transplanted with a deceased donor [cs-HR: 1.31, 95% CI: (1.00–1.71)]. For patients transplanted with a living donor, after adjusting for graft age, cardiovascular history, respiratory failure, age and BMI of the donor, there was no association between the EDI and death (Table 2).

Using the Fine and Gray model, patients of the quintile 5 had a significantly higher risk of death than those of the quintile 1 both in the complete cohort [sd-HR: 1.29, 95% CI: (1.00–1.68)] and in the cohort transplanted with a deceased donor [sd-HR: 1.30, 95% CI: (1.00–1.70)]. In the living donor population, no association was observed between EDI quintiles and death [quintile 2: 0.36 (0.07–1.85), quintile 3: 0.68 (0.17–2.71), quintile 4: 0.61 (0.15–2.43) and quintile 5: 1.37 (0.48–3.93)].

The trend test was statistically significant when the EDI quintiles were entered in the Cox and Fine and Gray models as ordinal covariate for the complete cohort [cs-HR: 1.08 (1.02–1.14), sd-HR: 1.07 (1.01–1.13), respectively] and for the cohort of patients transplanted with a deceased donor [cs-HR: 1.07 (1.01–1.13), sd-HR: 1.07 (1.01–1.13), respectively] (Tables 2 and 3).

EDI and risk of renal transplant failure

Of the 8701 patients, 784 had a transplant failure during the study period (probability of the event at 48 months: 8.89%). Cumulative incidence curve of transplantation failure is displayed in Fig. 2. Regardless of donor type, after adjusting for graft recipient age, cardiovascular and respiratory insufficiency, diabetes, causal nephropathy, dialysis modalities, duration of dialysis, type of tobacco consumption and delayed resumption of renal graft function, multivariable analysis with the Cox model and the Fine and Gray model did not show any association between the EDI entered in the model as a categorical covariate or as an ordinal covariate and the risk of renal graft failure (Tables 2 and 3).

Discussion

This study shows that in France, social deprivation is common in patients who have received a renal transplant since 32% of the individuals were classified in the quintile 5 of the general population, that is the most

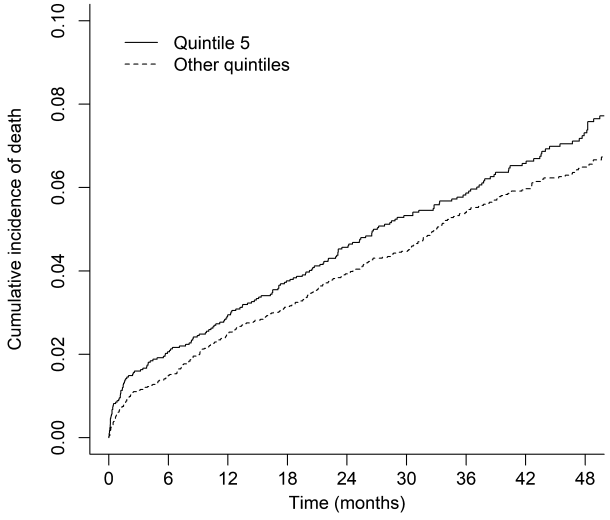

Figure 1 Cumulative incidence of death by quintiles.

Table 2. Association between the European Deprivation Index and the outcome on transplantation (multivariate analysis with a Cox model).

	Death [cs-HR (95% CI)]						Graft loss [cs-HR (95% CI)]					
	Complete cohort		Excluding living donor		Living donor		Complete cohort		Excluding living donor		Living donor	
EDI	Trend*	Quintiles*	Trend†	Quintiles†	Trend‡	Quintiles‡	Trend§	Quintiles§	Trend¶	Quintiles¶	Trend**	Quintiles**
Q 1	1.08	Ref	1.07	Ref	1.16	Ref	0.97	Ref	0.97	Ref	1.04	Ref
Q 2	[1.02–1.14]	1.00 [0.73–1.36]	[1.01–1.13]	1.05 [0.77–1.44]	[0.87–1.55]	0.36 [0.07–1.90]	[0.93–1.02]	0.89 [0.70–1.15]	[0.92–1.02]	0.87 [0.67–1.14]	[0.86–1.26]	1.00 [0.35–2.61]
Q 3	*P* trend	1.17 [0.87–1.56]	*P* trend	1.20 [0.89–1.62]	*P* trend	0.70 [0.16–2.94]	*P* trend	0.95 [0.75–1.22]	*P* trend	0.92 [0.72–1.19]	*P* trend	1.31 [0.52–3.30]
Q 4	= 0.01	1.21 [0.91–1.61]	= 0.02	1.26 [0.94–1.69]	= 0.31	0.62 [0.16–2.32]	= 0.28	0.86 [0.67–1.09]	= 0.22	0.84 [0.65–1.08]	= 0.67	0.90 [0.35–2.29]
Q 5		1.31 [1.01–1.70]		1.31 [1.00–1.71]		1.39 [0.47–4.12]		0.88 [0.71–1.10]		0.86 [0.69–1.07]		1.26 [0.53–3.04]

*Adjusted on recipient age at transplantation, recipient gender, nephropathy, diabetes, cardiovascular disease, chronic pulmonary disease, hepatitis C, dialysis modality, dialysis duration, donor source, tobacco, recipient BMI, delayed graft function.

†Adjusted on recipient age at transplantation, recipient gender, nephropathy, diabetes, cardiovascular disease, chronic pulmonary disease, hepatitis C, dialysis modality, dialysis duration, donor source, tobacco, recipient BMI, delayed graft function, donor with diabetes, donor with hypertension.

‡Adjusted on recipient age at transplantation, cardiovascular disease, chronic pulmonary disease, donor age, donor BMI.

§Adjusted on recipient age at transplantation, nephropathy, diabetes, cardiovascular disease, chronic pulmonary disease, dialysis modality, dialysis duration, donor source, tobacco, delayed graft function.

¶Adjusted on recipient age at transplantation, nephropathy, cardiovascular disease, chronic pulmonary disease, tobacco, delayed graft function, donor age, donor with diabetes, donor with hypertension, cause of death.

**Adjusted on nephropathy, chronic pulmonary disease, delayed graft function.

Table 3. Association between the European Deprivation Index and the outcome on transplantation (multivariate analysis with a Fine and Gray model).

	Death [sd-HR (95% CI)]						Graft loss [sd-HR (95% CI)]					
	Complete cohort		Excluding living donor		Living donor		Complete cohort		Excluding living donor		Living donor	
EDI	Trend*	Quintiles*	Trend†	Quintiles†	Trend‡	Quintiles‡	Trend§	Quintiles§	Trend¶	Quintiles¶	Trend**	Quintiles**
Q 1	1.07	Ref	1.07	Ref	1.16	Ref	0.96	Ref	0.96	Ref	1.04	Ref
Q 2	[1.01-1.13]	1.03 [0.76–1.40]	[1.01–1.13]	1.08 [0.79–1.48]	[0.84–1.59]	0.36 [0.07–1.85]	[0.92–1.01]	0.90 [0.69–1.16]	[0.91–1.01]	0.87 [0.67–1.14]	[0.85–1.27]	0.95 [0.32–2.82]
Q 3	*P* trend	1.17 [0.87–1.56]	*P* trend	1.21 [0.89–1.63]	*P* trend	0.68 [0.17–2.71]	*P* trend	0.94 [0.73–1.21]	*P* trend	0.91 [0.70–1.17]	*P* trend	1.32 [0.51–3.36]
Q 4	=0.02	1.21 [0.91–1.60]	=0.03	1.26 [0.94–1.69]	=0.37	0.61 [0.15–2.43]	=0.17	0.84 [0.65–1.08]	=0.11	0.81 [0.63–1.05]	=0.72	0.90 [0.34–2.39]
Q 5		1.29 [1.00–1.68]		1.30 [1.00–1.70]		1.37 [0.48–3.93]		0.86 [0.69–1.07]		0.83 [0.66–1.04]		1.22 [0.49–3.08]

*Adjusted on recipient age at transplantation, recipient gender, tobacco, recipient BMI, nephropathy, recipient diabetes, cardiovascular disease, chronic pulmonary disease, hepatitis C, dialysis modality, dialysis duration, delayed graft function, miss match DR, donor BMI, donor age, cause of death, donor with hypertension, donor with diabetes.

†Adjusted on recipient age at transplantation, cardiovascular disease, chronic pulmonary disease, donor age, donor BMI.

‡Adjusted on nephropathy, delayed graft function.

§Adjusted on recipient age at transplantation, recipient gender, tobacco, recipient BMI, nephropathy, recipient diabetes, cardiovascular disease, chronic pulmonary disease, hepatitis C, dialysis modality, dialysis duration, delayed graft function, miss match DR, donor BMI, donor age, cause of death, donor with hypertension, donor with diabetes.

¶Adjusted on recipient age at transplantation, cardiovascular disease, chronic pulmonary disease, donor age, donor BMI.

**Adjusted on nephropathy, delayed graft function.

deprived class in the French population. This finding may be explained by the fact that social deprivation is both a cause and a consequence of chronic diseases [12]. Our study also suggests that, in transplanted patients, social deprivation is associated with female gender, age, diabetes and hepatitis C. This could be explained by the fact that, in France, income is unequal between men and women and among the different age groups [13,14]. In France, a relationship has been demonstrated between female sex and reduced access to the waiting list for renal transplantation, social deprivation that is more frequent in female could partly explain this finding [15]. Many barriers such as socio-economic or marital status and specific women's perception and women age may influence women access to kidney transplantation [16]. A recent study has suggested that the transplant team do not have the perception of the gender disparities and should collaborate with dialysis staff to improve women's access to kidney transplantation [17]. Further studies are needed as there is no clear explanation regarding gender disparity in France. A French study conducted in 2006 showed that the prevalence of hepatitis C was associated with exposure to social deprivation [18]. Furthermore, diabetes is a more frequent disease in socially deprived populations [19].

The univariable analysis suggested that patients who are more prone to social deprivation benefit less frequently from a renal transplant prior to dialysis than other patients. In a study about pre-emptive registration on the waiting list for renal transplantation that was conducted in the northwestern region of France, an association was observed between social deprivation evaluated by the EDI and the access to the waiting list before dialysis [20]. The association between social deprivation and pre-emptive transplantation requires further investigation.

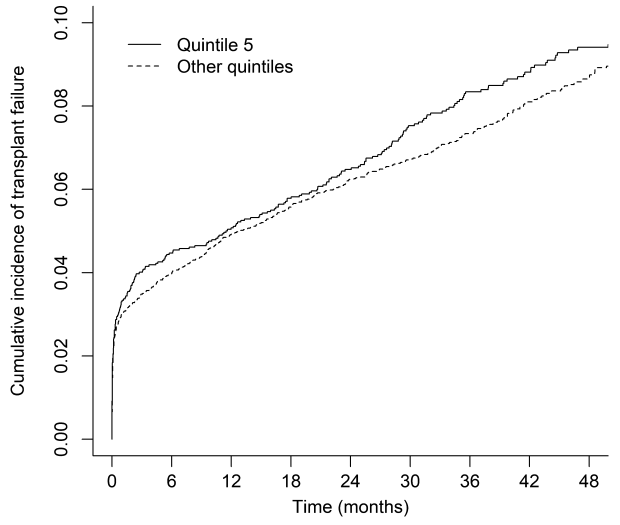

Figure 2 Cumulative incidence of transplantation failure by quintiles.

In our study, a Cox model was used to estimate the effect size of the EDI on the outcome, and a Fine and Gray model was utilized to evaluate the prognosis of individual exposed to deprivation measured by the EDI. Data from this comprehensive national cohort of renal transplant patients show that there is an association between the risk of death on transplantation and social deprivation as measured by the EDI. Contrary to what has been observed in the United States and the United Kingdom, there is no association in France between social deprivation and renal transplant failure, as defined by a return to dialysis or a second transplant. In the United States, although access to health care is guaranteed for Americans affiliated with the Veterans Department, ethnic disparities, which are often associated with social deprivation, are associated with transplant failure [21]. In the United States, the financial cost of immunosuppressant treatment was covered until recently by health insurance only for the first 36 months after transplantation. Thereafter, the treatment, which is very expensive, must be paid for by patients [22]. It has been shown that 24–41% of transplant patients face financial difficulties, which could influence the regular taking of treatments [23]. Since 2010, the American healthcare system has been modified to improve the quality of care and access to the healthcare system, making it possible to pay for immunosuppressive treatment for all transplant patients. For several decades, the French healthcare system has included a specific coverage called 'Affection de Longue Durée' that provides total reimbursement of medical expenses related to chronic diseases, including chronic kidney disease and renal transplantation. For individuals without health insurance, financial coverage is provided by a universal health coverage 'Couverture Médicale Universelle' [24]. It is possible that complete financial coverage explains the lack of association between social deprivation and renal transplant failure. Access to social protection rights is guaranteed for the vast majority of the French population. However, access to secondary care is still subject to inequalities due to lack of knowledge of the health system, thus reflecting a level of 'health culture' that can be linked to SIH. The lack of care, the perceived complexity of administrative procedures and insufficient preventive care could have an impact on the health status of socially deprived people [25]. In France, SIH have been shown to influence the health of

individuals exposed to social deprivation from the earliest age, resulting in a 7-year difference in life expectancy at age 35 between workers and senior managers [26]. Social inequalities in mortality are higher in France than in other European countries and have tended to increase in recent years [27]. In our study, the gradual increase in the risk of death among the different EDI quintiles in subjects receiving a renal transplant may reflect the effect of the social gradient of socially constructed inequalities in the general population beginning before renal transplantation. In both the United States and the United Kingdom, SIH measured by an aggregate social deprivation index have been associated with an increased risk of renal transplant death [9,28]. In addition, the distance between patient home and the transplant centre that is associated with a higher risk of mortality raises the question of the isolation of socially deprived populations [29]. Our study shows that in France, foreign-born transplanted patients are more likely to be exposed to social deprivation than the other patients. In the United States where ethnicity is a marker of social deprivation [30], it has been shown that Afro-American or Hispanic have a higher risk of mortality and morbidity than white subjects [13].

The impact of SIH on transplantation outcome raises the issue of how health inequalities related to social status may be measured, as the concept of social deprivation is multidimensional. At the individual level, socio-economic status is generally explored by the income, the education level and the work status. In the absence of individual data, the EDI is a powerful tool for assessing social deprivation using ecological data related to the place of residence and its influence on health [3]. The EDI is assessed at the level of the IRIS, the smallest geographical unit in France, that is municipalities with fewer than 2000 inhabitants. Unlike other ecological indices, its construction is transposable in 26 European countries, as it is based on an EU-SILC study with a selection of variables reflecting the perception of social deprivation, which differs from country to country. It is therefore possible to use the EDI to compare the potential impact of health systems in European countries on renal transplantation. Such a comparison should make it possible not only to better understand the mechanisms of social inequalities in renal transplantation but also to prevent the effects of SIH by intervening early in the trajectories of patients with chronic kidney disease.

There are limitations in our study; residual confounders, not captured in the registry, may affect the outcome on renal transplantation; in addition, covariates were registered at registration on the waiting list. The EDI, calculated at the patient registration, may have changed during the time spent on dialysis or on the waiting list. In addition, long-term survival of the allograft was not evaluated since the length of the follow-up was limited to 6 years. The distance between patient home and transplant centre, which may affect the outcome on transplantation, was not evaluated in our study. There was an ecological bias as the EDI is a proxy of individual deprivation at the IRIS level. Nevertheless, the IRIS is the smallest geographical area identified in France, IRIS corresponded to 2000 inhabitants (49989 IRIS in France). Thus, the size of the IRIS limits the importance of the ecological bias.

In conclusion, this study shows that, in France, social deprivation estimated by the EDI is associated with an increased risk of death on transplantation but that there is no link between social deprivation and the risk of graft loss. The EDI allows comparisons between European countries and should be the subject of further investigations.

Authorship

VC and TL: performed the research, analysed data, collect data and wrote manuscript. SB-M, CV: reviewed the manuscript. GL: performed the EDI calculation.

Funding

The study was funded by a grant of the 'Agence de la Biomédecine'.

Conflict of interest

The authors do not have any conflict of interest.

REFERENCES

1. Whitehead M, Dahlgren G. What can be done about inequalities in health? *Lancet* 1991; **338**: 1059.
2. Hörl WH, de Alvaro F, Williams PF. Healthcare systems and end-stage renal disease (ESRD) therapies-an international review: access to ESRD treatments. *Nephrol Dial Transplant* 1999; **14**: 10.

3. 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.
4. Guillaume E, Pornet C, Desjardins O, *et al.* Development of a cross-cultural deprivation index in five European countries. *J Epidemiol Community Health* 2016; **70**: 493.
5. Bryere J, Pornet C, Copin N, *et al.* Assessment of the ecological bias of seven aggregate social deprivation indices. *BMC Public Health* 2017; **17**: 86.
6. Bryere J, Dejardin O, Bouvier V, Colonna M, Guizard AV, Troussard X. Socioeconomic environment and cancer incidence: a French population-based study in Normandy. *BMC Cancer* 2014; **14**: 87.
7. Goldfarb-Rumyantzev AS, Koford JK, Biaird B, Wang BJ, Lin S, Isaacs RB. The role of socioeconomic status in kidney transplant outcome. *Clin J Am Soc Nephrol* 2006; **1**: 313.
8. Hod T, Goldfarb-Rumyantzev AS. The role of disparities and socioeconomic factors in access to kidney transplantation and its outcome. *Ren Fail* 2014; **36**: 1193.
9. Begaj I, Khosla S, Ray D, Sharif A. Socioeconomic deprivation is independently associated with mortality post kidney transplantation. *Kidney Int* 2013; **84**: 803.
10. Kihal-Talantikite W, Vigneau C, Deguen S, Siebert M, Couchoud C, Bayat S. Influence of socio-economic inequalities on access to renal transplantation and survival of patients with end-stage renal disease. *PLoS One* 2016; **11**: e0153431.
11. Noordzij M, Leffondre K, van Strale KJ, Zoccali C, Dekker FW, Jager KJ. When do we need competing risks method for survival analysis? *Nephrol Dial Transplant* 2013; **28**: 2670.
12. Young EW, Mauger EA, Jiang KH, Port FK, Wolfe RA. Socioeconomic status and end-stage renal disease in the United States. *Kidney Int* 1994; **45**: 907.
13. Mackenbach JP, Stirbu I, Roskam AJ, *et al.* Socioeconomic inequalities in Health in 22 European Countries. *N Engl J Med* 2008; **358**: 2468.
14. Mandel H, Smyonov M. Gender pay gap and employment sector: sources of earnings disparities in the United States, 1970–2010. *Demography* 2014; **51**: 1597.
15. Couchoud C, Bayat S, Villar E, Jacquelinet C, Ecochard R, on behalf of the REIN registry. A new approach for measuring gender disparity in access to renal transplantation waiting lists. *Transplantation* 2012; **94**: 513.
16. Segev DL, Kucirka LM, Oberai PC, *et al.* Age and comorbidities are effect modifiers of gender disparities in renal transplantation. *J Am Soc Nephrol* 2009; **20**: 621.
17. Lipford KJ, McPherson L, Hamoda R, *et al.* Dialysis facility staff perceptions of racial, gender, and age disparities in access to renal transplantation. *BMC Nephrol* 2018; **19**: 5.
18. Meffre C, Le Strat Y, Delarocque-Astagneau E, *et al.* Prevalence of hepatitis B and hepatitis C virus infections in France in 2004: social factors are important predictors after adjusting for known risk factors. *J Med Virol* 2010; **4**: 546.
19. Saydah S, Lochner K. Socioeconomic status and risk of diabetes-related mortality in the U.S. *Public Health Rep* 2010; **125**: 377.
20. Riffaut N, Lobbedez T, Hazzan M, *et al.* Access to preemptive registration on the waiting list for renal transplantation: a hierarchical modeling approach. *Transpl Int* 2015; **28**: 1066.
21. Chakkera HA, O'Hare AM, Johansen KL, *et al.* Influence of race on kidney transplant outcomes within and outside the department of veterans affairs. *J Am Soc Nephrol* 2005; **16**: 269.
22. 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; **13**: 1358.
23. Gill JS, Tonelli M. Penny wise, pound foolish? Coverage limits on immunosuppression after transplantation kidney. *N Engl J Med* 2012; **366**: 586.
24. Grignon M, Perronin M. Impact de la couverture maladie universelle complémentaire sur les consommations de soins. *Question d'économie de la santé* 2003; **74**: 1.
25. Lombrail P, Pascal J. Inégalités sociales de santé et accès aux soins. *Les tribunes de la santé* 2005; **8**: 31.
26. Blanpain N. L'espérance de vie s'accroît, les inégalités sociales face à la mort demeurent. *INSEE Première* 2011; **1372**: 1.
27. Haut Conseil de la Santé Publique. *Les inégalités sociales de santé: sortir de la fatalité*. La Documentation Française: HCSP, 2009: 1–100.
28. Jordan H, Roderick P, Martin D. The Index of Multiple Deprivation 2000 and accessibility effects on health. *J Epidemiol Community Health* 2004; **58**: 250.
29. Axelrod DA, Dzebisashvili N, Schnitzler MA, et al. The interplay of socioeconomic status, distance to center, and interdonor service area travel on kidney transplant access and outcomes. *Clin J Am J Soc Nephrol* 2010; **5**: 2276.
30. Patzer RE, Mohan S, Kutner N, McClellan WM, Amaral S. Racial and ethnic disparities in pediatric renal allograft survival in the United States. *Kidney Int* 2015; **87**: 584.