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PEOPLE LIVING WITH HIV IN FRANCE HAVE DELAYED ACCESS TO KIDNEY TRANSPLANTATION

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Background

- Kidney transplantation (KT) is associated with a better survival than hemodialysis in selected end-stage renal disease (ESRD) patients:
  - in the general population,
  - in people living with HIV (PLHIV).
- Because of potent antiretroviral therapy (ART) availability, the number of KT increases over time in PLHIV since the early 2000s
- Transplant survival is close to the kidney transplant survival in HIV uninfected people aged at least 65 years.
- Survival of PLHIV after KT is comparable to survival of HIV uninfected people.
- A lower access to KT in PLHIV has recently been described in the US (Locke JE, Clin J Am Soc Nephrol 2017).
- Even in the context of free access to health care, nephrologists might be reluctant to KT in PLHIV because of potential interactions between antiretroviral and immunosuppressive drugs, fear of lower adherence rate or of higher risk of infection due to immunosuppression.

Objectives

- To investigate the impact of HIV infection on the access to the KT waiting list and on the access to KT in France.

Methods

Population

- From the **Renal Epidemiology and Information Network** (national registry of all patients dialysis) in France.
- Adults ≥ 18 years, initiating dialysis between January 2006 and December 2010.
- Exclusion criteria : ongoing cancer, previous KT, need of a combined solid organ transplantation.
- **Each PLHIV matched with one or two HIV uninfected individuals** on age (+/- 3 years), sex, year of dialysis initiation, diabetic nephropathy, and continent of birth whenever possible.
- HIV-specific data (ART, HIV viral load (VL), CD4 cell count) were extracted from the **French Hospital Database on HIV** (FHDH ANRS-CO4).

Methods

Statistical analysis

- Follow-up until December 31, 2015.
- **Cumulative incidence of enrolment on a KT waiting list** after dialysis initiation; with prelisting death as a competing risk
- **Cumulative incidence of KT** after enrolment on a waiting list; with postlisting death as a competing risk
- **Effect of HIV infection on the access to KT waiting list and on the access to KT** after enrolment on a waiting list assessed by using univariable and multivariable **competing risk regression models**:
  - **Adjustment on** age, sex, geographical origin (sub-Saharan Africa vs other), diabetic nephropathy, period of dialysis initiation (2006-2008 vs 2009-2010) , initial dialysis modality, region of care (Paris area vs other), chronic hepatitis C and the number of severe conditions (malnutrition, cirrhosis, chronic cardiac failure, coronary heart disease, vascular disease, chronic respiratory failure).
  - **For the model used to study the access to KT, additional adjustment on** dialysis duration before waitlisting, blood group (A vs other) and the incompatible transplant rate (percentage of kidneys retrieved in the previous 5 years against which a given potential recipient has at least one significant anti-HLA donor-specific antibody).
  - **Change of care of PLHIV over time investigated** by the mean of testing for a potential interaction between infection status and the period of dialysis initiation.
- **Sensitivity analyses** among:
  - PLHIV treated with ART,
  - PLHIV with CD4 > 200/mm3 and VL<500 cp/ml on ART (immunovirological control),

  and their matched controls.

Results

- **255 PLHIV and 476 matched HIV uninfected controls** were included:
  - . **Median follow-up** : 5.6 (3.0-7.2) and 6.3 (5.0-7.9) years respectively
  - . 69% male, median age 47 (41-58), 18% born in sub-Saharan Africa, 41% dialysis initiation in 2009-10
  - . Information on HIV infection for 180 PLHIV (70.6%):
    - 176 (97.8%) on antiretroviral therapy while on dialysis
    - 105 (74.0%) with immunovirological control on ART among 142 patients with data

Table 1. Characteristics of PLHIV and their controls at dialysis initiation

	PLHIV N = 255	HIV uninfected N = 476	p
Initial dialysis modality			0.02
Hemodialysis	238 (93.3%)	418 (87.8%)	
Peritoneal dialysis	17 (6.7%)	58 (12.2%)	
Dialysis in Paris area	165 (64.7%)	166 (34.9%)	<0.0001
Hypertension	173 (70.0%)	370 (80.0%)	0.003
Diabete mellitus	57 (22.5%)	94 (19.8%)	0.39
Chronic hepatitis C	49 (19.8%)	14 (3.0%)	<0.0001
Malnutrition (BMI<18.5 kg/m² or alb.<27g/l)	61 (25.1%)	65 (14.2%)	0.0002
Number of comorbidities			0.02
0	119 (50.6%)	272 (60.4%)	
1	80 (34.0%)	104 (23.1%)	
≥ 2	36 (15.4%)	74 (16.5%)	
Hemoglobin (g/dl)	11.0 (10.0-12.0)	11.3 (10.3-12.3)	0.04

Table 2. multivariable competing risk regression analyses of the effect of HIV infection on the access to KT waiting list and on the access to KT

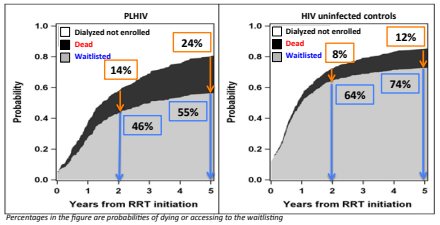
Waiting list enrolment or death: 255 PLHIV and 476 HIV uninfected individuals	Waiting list enrolment sdHR* (95%CI)	p	Prelisting mortality sdHR* (95%CI)	p
HIV infection (ref HIV uninfected)				
dialysis initiation in 2006-2008	0.43 (0.33-0.56)	<0.0001	2.23 (1.50-3.36)	<0.0001
dialysis initiation in 2009-2010	0.66 (0.47-0.93)	0.02	1.37 (0.67-2.81)	0.39

KT or death after waiting list: 149 PLHIV and 348 HIV uninfected individuals	Kidney transplantation sdHR**(95%CI)	p	Postlisting mortality sdHR** (95%CI)	p
HIV infection (ref HIV negative people)	0.71 (0.54-0.92)	0.01	0.90 (0.37-2.17)	0.82

*adjusted on age, sex, geographical origin, diabetic nephropathy, initial dialysis modality, region of care, chronic hepatitis C and number of severe conditions, ** same adjust' plus period of dialysis initiation, duration on waitlisting, blood group and the incompatible transplant rate

Similar results when analyses were restricted to:
- HIV-infected individuals on ART,
- or HIV-infected individuals with immunovirological success on ART

Figure. Cumulative incidence of enrolment on a waiting list or death after dialysis initiation for PLHIV and for HIV uninfected individuals



Percentages in the figure are probabilities of dying or accessing to the waitlisting

Five years probabilities of KT or death after enrolment on a waiting list:
59% and 10% among PLHIV
83% and 4% among HIV-uninfected controls

Discussion

- Among patients initiating dialysis in France between 2006 and 2010 and followed until the end of 2015, **PLHIV had lower rates of enrolment on KT waiting list and of KT** than their matched HIV uninfected controls.
- Similar results were observed when analyses were restricted to PLHIV with immunovirological success on ART.
- Despite an improvement over time, access to the waiting list was still lower in the most recent period where ART with lower interaction with immunosuppressive drugs is available.
- We were not able to assess psychosocial factors that might have impaired access to waiting list or to KT in PLHIV. However models were adjusted on hepatitis C more frequent in PLHIV which could act as a surrogate marker for intravenous drug use.
- There were no differences in prelisting mortality in the recent period or in postlisting mortality in PLHIV compared to HIV uninfected individuals.

Conclusion

- The reasons for an impaired access of PLHIV to KT must be explored.
- HIV practitioners and nephrologists need to be informed about the benefits of KT over dialysis for PLHIV.