

ERA Long-Term Research Fellowship Project

EUDIAL & DESCARTES

Project's key info

Title of the project	Return to dialysis after kidney transplant failure: typical profiles and impact of immunosuppression strategies on the hazard of hospitalisation, death and retransplantation
Working Group involved in the project	European Dialysis Working Group (EuDial) & Developing Education Science and Care for Renal Transplantation in European States Working Group (DESCARTES)
Principal Investigator(s) of the project	Christian Combe (France) Christophe Mariat (France)
Duration	12 months
Fellowship Grant	34.495,00 €
Start of the fellowship	Within 6 months after notification of the grant award to the fellow.

Receiving Institute

Name of receiving institute	Bordeaux Population Health, INSERM U1219 Research Centre
Supervisor's name	Christian Combe (France) Christophe Mariat (France)
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Project's detailed description

<p>Project description</p> <p>Kidney transplantation is the best treatment for patients with Kidney Failure, but long-term graft survival remains suboptimal, return to dialysis is a frequent event. For instance, in France in 2022, 1101 patients returned to dialysis because of allograft failure, representing 8.7% of incident dialysis patients. This transition period is associated with an increased hazard of infections, cardiovascular events, death, and lower quality of life. The management of patients returning to dialysis is unfortunately not straightforward and prompt to significant heterogeneity in clinical practice^o, for instance on the decision to taper or withdraw immunosuppression after dialysis initiation, or on the issue of transplantectomy. As recently highlighted in the KDIGO controversies conference, the return to dialysis in patient with failed allograft must benefit from individualization but suffers from a serious lack of data. The first objective of the project will be to identify patients' characteristics and trajectories associated with increased hazards of hospitalisation and death.</p>

In a second step, the project aims to evaluate the impact of different strategies of immunosuppression and of transplantectomy, on mortality, hospitalization and retransplantation among these newly identified profiles of patients.

Methods

Population: The project will study French patients returning to dialysis between 2015 and 2020 because of first kidney allograft failure, after at least 3 months of function.

Data sources and covariates: This project will be based on the French REIN registry which collects data on all patients on renal replacement therapy in France and the Système National des Données de Santé (SNDS), a French nationwide medico-administrative healthcare database which collects information on hospitalisations, medical procedures, medications, and all expenses covered by the National Health Insurance system. Hence, we will be able to retrieve a large collection of data including:

- Demographic, socioeconomic, clinical and biological data;
- Characteristics of kidney allograft;
- Specific events (consultation, vascular access; intervention, hospitalization, retransplantation, death, professional timeline...) occurring during follow-up;
- Medications from functioning kidney graft to return to dialysis including immunosuppression treatment;
- Transplantectomy after return to dialysis.

The combined use of data from the REIN registry and the SNDS is unique to France, this work cannot be done at the European level for instance.

Outcomes: The study will include events occurring in the 3-years after returning to dialysis:

- All-cause death
- Hospitalization for cardiovascular, infectious or cancer events
- Retransplantation

Statistics: This work will require the use of sophisticated statistical tools. To identify typical profile of patients returning to dialysis associated with different risks of events we will use methods of classification adapted to multidimensional data. We intend to use in particular Bayesian profile regression mixture models. Due to the large number of potentially variables associated with the risk of events of interest, we may use, in a previous step, selection methods such as random forest for survival data in order to identify the most important predictors of events. To assess the hazard of hospitalization for cardiovascular, infectious or neoplastic causes, mortality and retransplantation, we will perform a target trial emulation that will test the impact of different immunosuppression strategies and of transplantectomy. This is a very important clinical question that has not been addressed yet by randomised trials to our knowledge. Given the number of patients with failed allograft returning to dialysis each year in France (=1000 patients/year) we anticipate having the required sample size to perform this project.

Expected impact: The research team believes that this work will contribute to improve knowledge about the critical period of return to dialysis after failed kidney allograft and will provide new insights and perspectives for improving care in those patients especially in the management of immunosuppression.

Goals of the project

The research project goals are the following:

- To identify and describe the typical profile of patients returning to dialysis after kidney transplant failure and estimate, for each profile, the hazard of hospitalization for cardiovascular, infectious or neoplastic causes and mortality;
- To assess the hazard of hospitalization for cardiovascular, infectious or neoplastic causes, mortality and retransplantation associated with different immunosuppression strategies and transplantectomy in patients returning to dialysis after kidney allograft failure in a target emulation trial

Qualifications and/or expertise required to the fellow

Requirements include:

- Qualification in epidemiology with strong skills in biostatistics
- Solid medical background
- Expertise in renal epidemiology