Development and Validation of a french kidney donor marginality score

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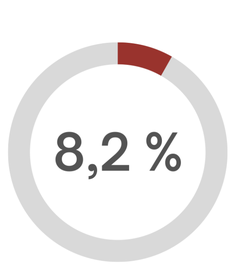
Background

- **Kidney transplantation** has been recognised as the best treatment for **end-stage chronic renal disease**
  - **Graft shortage** in countries with an aging population

  ⇒ Necessity for an expansion of the pool of available allografts
- Wide use of **marginal allografts** with suboptimal properties for patient-graft survival
- Decision making tools to assist clinicians in evaluating allograft proposals
  - **ECD Criterion (2002):** Binary criterion defining marginal donors as older than 60 years old or between 50 and 59 with at least 2 comorbidities among: high serum creatinine, history of hypertension and death by CVA

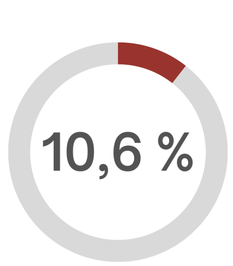
  ⇒ No gradient between less and more marginal donors
  - **KDRI/KDPI (2009):** Continuous/percentile scale defined by 10 donor features

⇒ Not adapted to the french population [5] and prone to an increased allograft refusal rate [3]



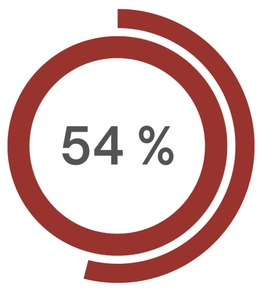
Chronic renal disease prevalence

In the 35-75 yo french population in 2015 [4] including asymptomatic forms



Mortality rate

In France in 2015 [1]



Increase in waiting list length

Between 2010 and 2015 in France despite an increase in transplanted allografts [2]

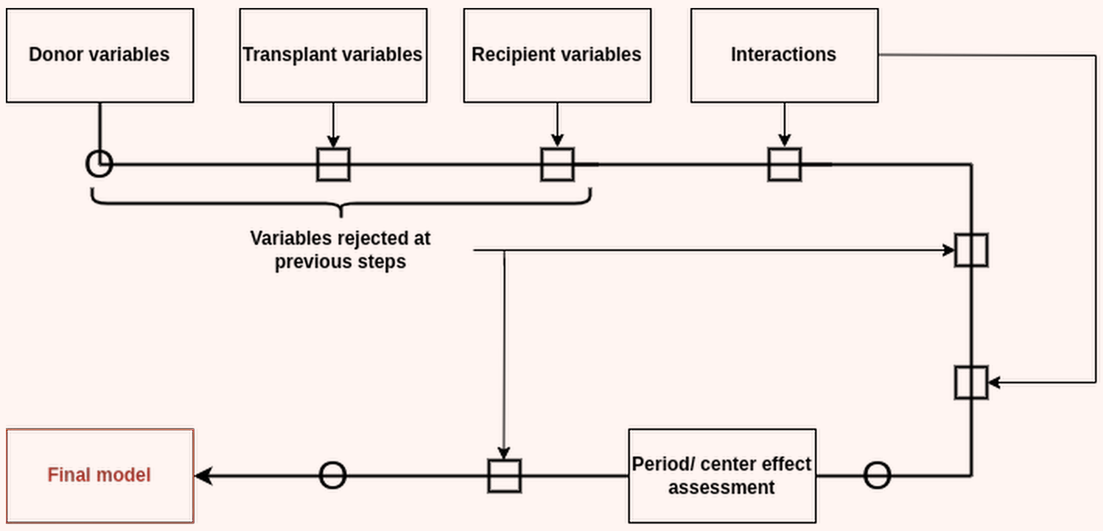
Objectives

Develop and validate a kidney donor marginality score that is **adapted to the french population** and **suited for the current practices** in kidney transplantation in France

- **Donor/recipient interactions** will be studied in order to express donor marginality in relation to recipient characteristics
- **External validation** could be performed and allow for an evaluation of the score's validity in other countries
- **Causal inference** could be used to estimate recipient loss-of-chance related to receiving a marginal allograft as defined by the proposed score

Materials and Methods

- **7622 patients** and 100 variables from the DIVAT national kidney transplant cohort
- First-time deceased donor allograft recipients without donor-recipient ABO incompatibility
- Analyses performed on **R version 4.3.0** and additional packages.
- **Multivariate Cox regression** model built via blockwise variable selection approach (Donor/Graft/Recipient features assessed separately, then jointly)
- Assessment of **period/center effect** via adjusted and frailty models



Variable selection process (square nodes indicate all previously included predictors were forced in the model during backward selection, circle nodes indicate no variable was forced)

- Validity assessed through:
  - **Calibration:** calibration plot, predicted survival by score quantile, Brier score
  - **Discrimination:** time-dependent ROC curve (AUC, PPV/NPV) and time-dependent ROC curve per recipient strata
- **Internal validation:** $\frac{1}{3}$ of the database allocated to a random validation sample
- **External validation:** using data from other DIVAT centers or an european cohort.
- **Sensitivity analysis:** Model compared to results from pliable LASSO and blockwise pliable LASSO procedures.

Results

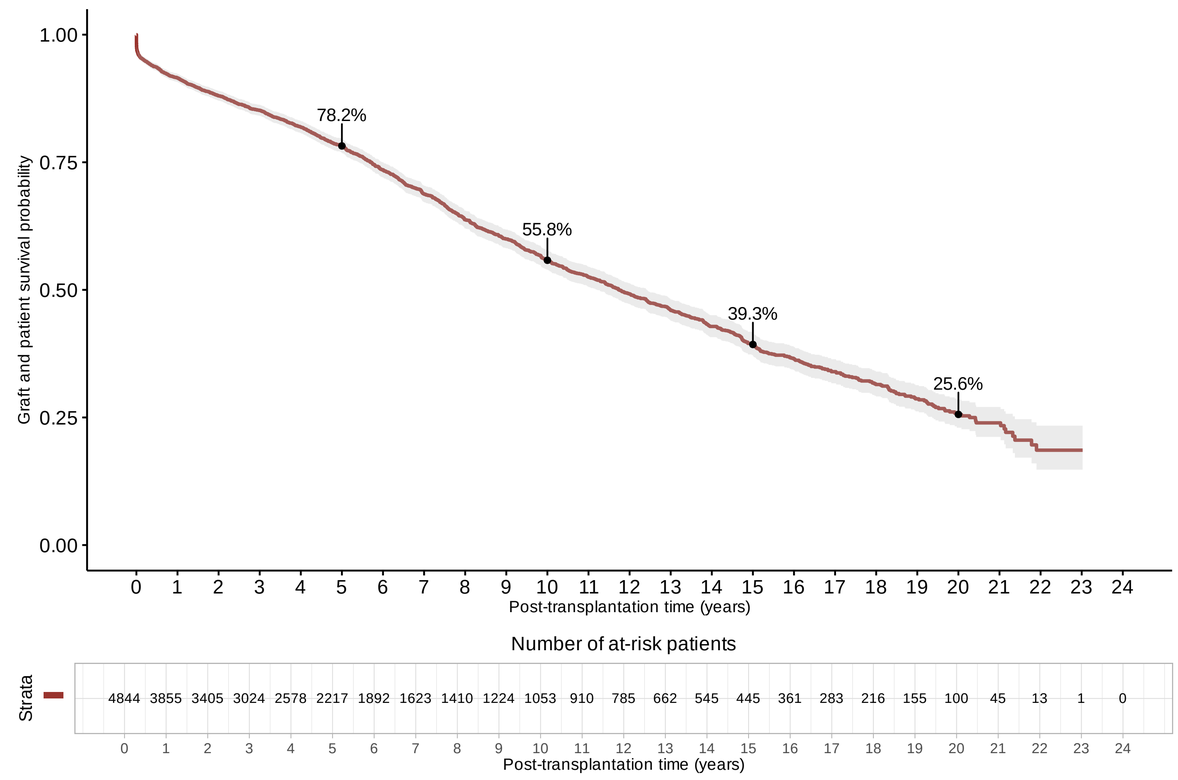


Figure 1. Patient/allograft survival analysis

	β	HR	95% CI	p
Donor age	-0.020			0.019
Donor after cardiac death	0.691	2.00	[1.51-2.63]	≤0.001
Donor death vascular etiology	-0.616			0.047
Donor creatinine	0.001	1.001	[1.001-1.002]	0.041
Donor height	-0.011	0.99	[0.98-0.99]	0.003
Donor weight	0.005	1.01	[1.001-1.01]	0.009
Positive donor CMV serology	0.124	1.13	[1.01-1.27]	0.031
HLA incompatibilities ≥4	0.151	1.16	[1.01-1.34]	0.038
Time on dialysis	0.0001	1.001	[1.001-1.001]	0.021
Transplanted before 2012	0.190	1.21	[1.04-1.40]	0.013
Recipient age	-0.021			0.008
Recipient BMI	0.011	1.01	[1.00-1.03]	0.116
Recipient history of diabetes	0.376	1.46	[1.26-1.68]	≤0.001
Recipient history of cardiovascular disease	0.408	1.50	[1.34-1.69]	≤0.001
Hemodialysis	0.250	1.28	[1.05-1.57]	0.015
Donor age*Recipient age	0.001			≤0.001
Donor death vascular etiology*Recipient age	0.014			0.011

Table 1. Proportional hazards Cox model analysis of retained factors and interactions after multivariate selection

- Donor age, beating heart status, cause of death, creatininemia, height, weight and CMV serology will be integrated into the score. For a given donor, the score will differ depending on recipient age and donor/recipient HLA ABDR incompatibilities.

What's next

- **Internal validation** of the model
- **External validation** of the model, if possible
- Definition of a **score computation formula** adapted to its potential use cases
- **Propensity score**-based analysis to estimate population-averaged effects and propose a recipient loss-of-chance-based approach
- Development of an **online score computation tool** for clinicians

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