Development and Validation of a french kidney donor marginality score

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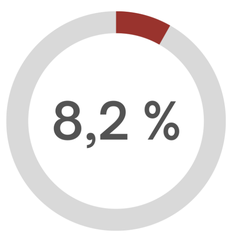
Background

- **Kidney transplantation (KT)**: recognised as the best treatment for **end-stage chronic renal disease**
  - **Graft shortage** in countries with aging population

  ⇒ Necessity for expansion of graft pool
- Wide use of **marginal grafts** with suboptimal properties for patient-graft survival
- Decision making tools to assist clinicians in evaluating graft proposals
  - **ECD [1]** 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

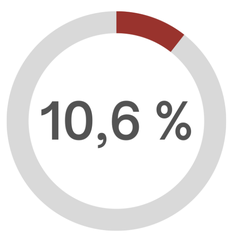
  ⇒ Binary criterion, no gradient between less and more marginal donors
  - **KDRI/KDPI [2]** Continuous/percentile scale defined by 10 donor features

  ⇒ Not adapted to the french population [3] and prone to increased graft refusal rate [4]



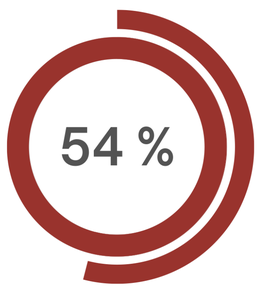
Chronic renal disease prevalence

In the 35-75 yo french population in 2015 [6] including asymptomatic forms



Mortality rate

In France in 2015, in patients with end-stage chronic renal disease [5]



Increase in waiting list length

Between 2010 and 2015 in France despite an increase in transplanted grafts [7]

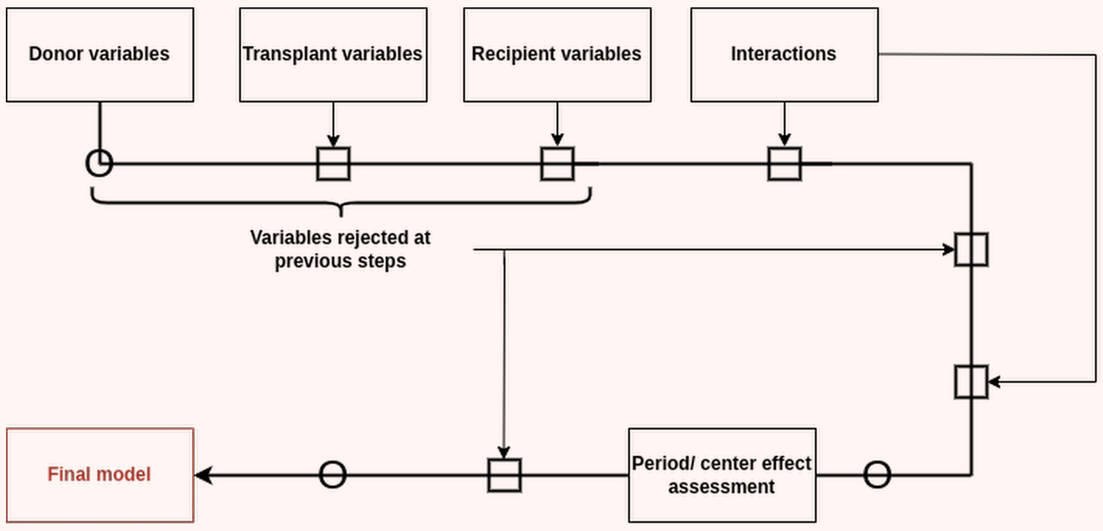
Objectives

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

- **Donor/recipient interactions** will be studied in order to express donor marginality in relation to recipient characteristics
- **Recipient loss-of-chance** related to receiving a marginal graft as defined by the proposed score will be studied

Materials and Methods

- **7622 patients** from the DIVAT national kidney transplant cohort
- First-time deceased donor graft recipients without donor-recipient ABO incompatibility
- **Multivariate Cox regression** model built via blockwise variable selection approach (Donor/Graft/Recipient features integrated/removed from the model in 11 steps)
- Assessment of **period/center effect** via adjusted and frailty models
- New variable selection steps after integration of period/center effects



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)

Results

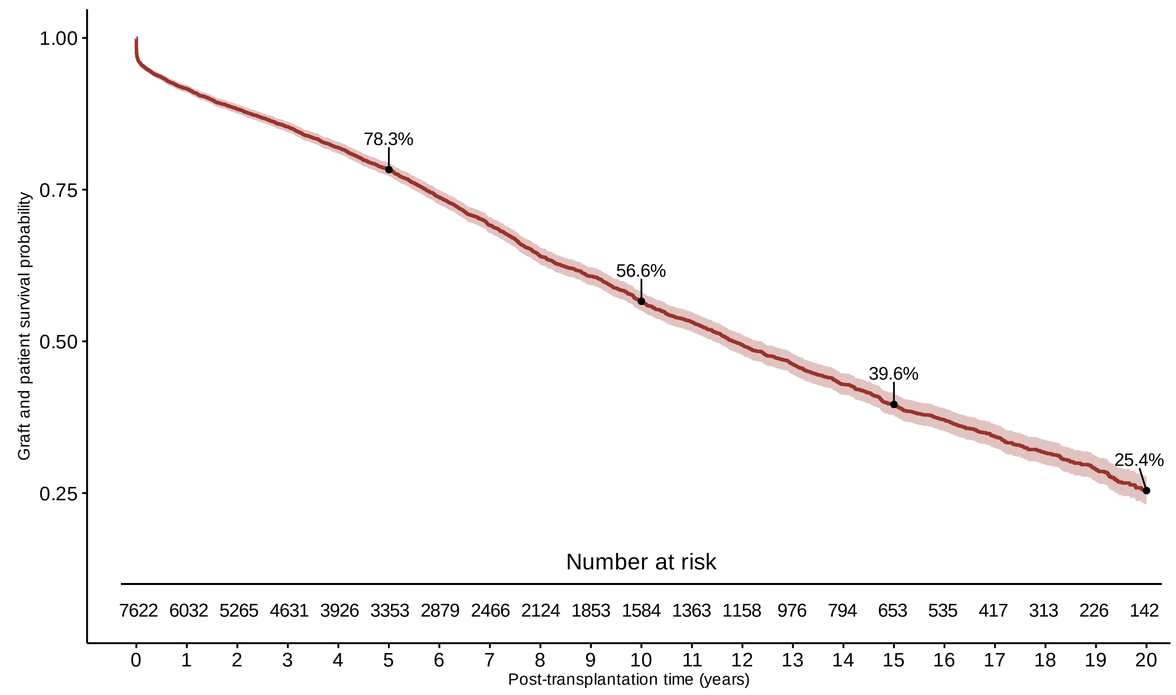


Figure 1. Patient/allograft survival analysis

	β	95% CI
Donor age	-0.020	[-0.037– -0.003]
Donor after cardiac death	0.691	[0.416–0.967]
Donor death by CVA	-0.616	[-1.224– -0.008]
Donor serum creatinine	0.001	[0.0001–0.002]
Donor height	-0.011	[-0.018– -0.004]
Donor weight	0.005	[0.001–0.010]
Positive donor CMV serology	0.124	[0.010–0.239]
HLA incompatibilities $\geq$4	0.151	[0.009–0.293]
Time on dialysis	0.0001	[0.0001–0.0001]
Transplanted before 2012	0.190	[0.040–0.340]
Recipient age	-0.021	[-0.036– -0.005]
Recipient BMI	0.011	[-0.003–0.025]
Recipient history of diabetes	0.376	[0.234–0.517]
Recipient history of cardiovascular disease	0.408	[0.239–0.527]
Hemodialysis	0.250	[0.048–0.452]
Donor age*Recipient age	0.001	[0.0001–0.001]
Donor death by CVA*Recipient age	0.014	[0.003–0.024]

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

- Donor age, beating heart status ($HR = 2.00$), cause of death, creatininemia, height, weight and CMV serology ($HR = 1.13$) 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, $\frac{1}{3}$ of the database allocated to a random validation sample
- **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
- **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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