In renal transplantation, early surveillance biopsies are becoming a current tool for the detection of histological lesions without associated clinical abnormality (1) but possible consequences on long-term prognosis. Despite the lack of specific recommendations, 3-months and/or 12-months surveillance biopsies are nowadays widely practiced by physicians in charge of kidney transplanted patients.

Nevertheless, surveillance biopsy remains debated after renal transplantation(2) since:
- Biopsy is an invasive chiral act exposing patients to risks of bleeding, bruise, infection, graft loss, etc.(3)
- Whatever the type of discovery on the surveillance biopsies (particularly at one year of follow-up), either normal or abnormal features, the histological diagnosis does not lead to clear therapeutic and consensual recommendations(4,5).
- Biopsy are "costly" for the patient since it generates a specific stress and for the society since it needs specific hospitalization.

Hypothesis: To practice a surveillance biopsy could sometimes be unnecessary since, among normal histology or low lesions of specific IFTA grade 1, benefit/risk balance is controversial (no evidence for a benefit of a therapeutic intervention but a risk for the kidney and the patient and a cost for the society).

Objectives
- To identify and validate a clinical diagnostic signature of histological lesions from surveillance biopsy at one year after renal transplantation
- In order to not propose surveillance biopsy to patients for whom it may be useless

Study population
Patients were selected from the 3 centers of the French prospective DIVAT cohort of transplanted patients who practice routinely the one year surveillance biopsy (Nantes, Lyon and Necker) (www.divat.fr)

Inclusion criteria :
- Adult recipients,
- Of Kidney or combined Kidney-Pancreas transplantation,
- Transplanted between 2006 and 2012,
- For the first or second times,
- From deceased donor,
- Alive with a functioning graft at one year post-transplantation
- With a complete Banff classification for the one year post-transplantation systematic biopsy,
- Without BKV infection in the first post-transplantation year

Definition of histological group of interest
All 12-months surveillance biopsies were retrospectively reclassified according to the predominant anamnato-pathologic diagnosis based on Banff 2013 criteria.

The main judgment criteria is the Histological group of interest defined according the possibility for a physician to take a medical decision:
- Interventional group: Patients displaying abnormal biopsies including isolated IFTA (grade 2 or 3), borderline changes, acute or chronic T-cell mediated rejection (TCMR), and acute or chronic antibody-mediated rejection (ABMR), recurrent or de novo glomerulopathy
- Non-interventional group: Patients with normal histology or IFTA grade 1

Clinical diagnostic score X
- Constituted of 8 covariates (no relevant clinical interaction were retained) including
  - Recipient serum creatinine at 3-months, 6-months, and 12-months,
  - Recipient and donor gender,
  - Daily anticoagulant immunization,
  - Dialysis technique before transplantation (extra-renal filtration vs. pre-emptive graft)
  - Graft type (Pancreas-Kidney vs. Kidney)
- AUC of ROC curve = 0.69
- For NPV=75%, discriminating threshold C = -0.31 leads to PPV=31%, Sensitivity=93%, Specificity=25%

Validation results
- Among 150 independent patients for whom the diagnostic score X can be calculated,
  - 61 patients (41%) had abnormal biopsies
  - 89 patients (59%) had normal histology or IFTA grade 1
- AUC of ROC curve = 0.64 (95%CI[0.55-0.73])

Diagnostic capacities of the clinical score are reasonable and validated

Medical decision making

In this study, we built a clinical score that may allow:
- To diagnose patients at high risk of normal histology or IFTA grade 1 lesions without information (i.e. Non-interventional group) with a very low risk of error (NPV=90%)
- To avoid useless biopsy in 15% of patients in whom probably no therapeutic change will follow as a consequence of this invasive intervention

Conclusions
In this study, we built a clinical score that may allow:
- To diagnose patients at high risk of normal histology or IFTA grade 1 lesions without information (i.e. Non-interventional group) with a very low risk of error (NPV=90%)
- To avoid useless biopsy in 15% of patients in whom probably no therapeutic change will follow as a consequence of this invasive intervention

References