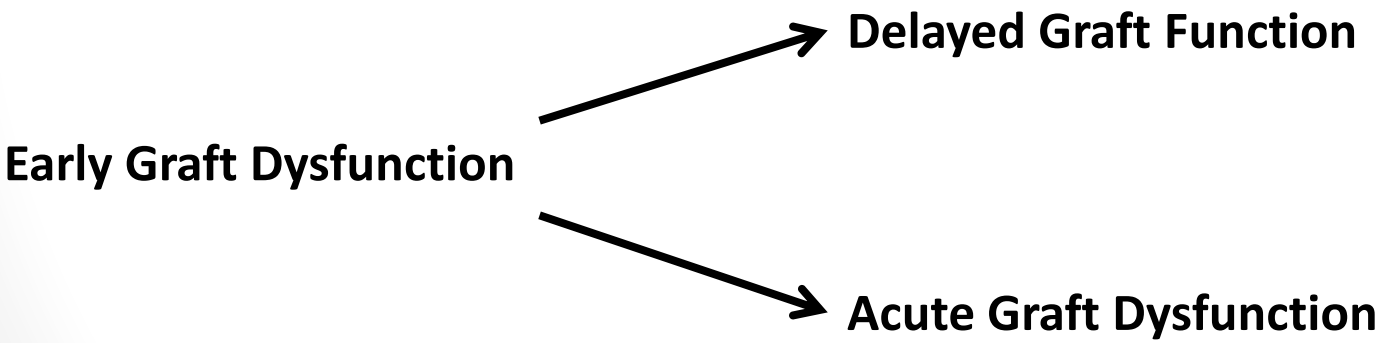
Investigating the threshold for early renal allograft biopsy

A South African single center perspective

D Nel, S Poerstamper, S Verhage, C Noel, F Botha, Z Barday, E Muller, T du Toit
Groote Schuur Hospital, University of Cape Town

Background

- Renal biopsy gold standard for diagnostic information post transplant
- Most common clinical indication for biopsy - early graft dysfunction



Commonest causes of EGD in first month post-transplant:

- Acute Tubular Necrosis (ATN)
- Cell-mediated rejection (CMR)
- Antibody mediated rejection (AMR)
- Calcineurin inhibitor toxicity (CNI)

Major complications of renal allograft biopsy:

- Need for interventional radiology procedures
- Operative exploration
- Graft loss
- Need for blood transfusion

- Unit historically maintained low threshold for allograft biopsy in setting of EGD
  - HLA mismatches have not been considered during deceased donor allocation
  - <2017 more restricted access to Tacro and MMF
  - <2018 no access to B-Cell CDC
  - High perceived rate of AR
  - Significant shortage of kidneys
  - Poor access to re-transplantation

    = Little margin for error

  - Recent literature suggests biopsy for EGD unnecessary - low rates AR with modern induction immunosuppression

Aim: To determine whether the current threshold for renal biopsy is appropriate in our setting, or whether the risks and complications of early renal allograft outweigh the benefits.

Methods:

- Retrospective audit at Groote Schuur Hospital
- Patients who underwent renal allograft biopsy within first 30 days of transplantation
- 1 June 2010 – 30 June 2018
- Exclusion criteria:
  - HIV positive to positive transplant biopsies
- Indications for biopsy:
  - Patients with significant EGD
    - DGF - dialysis D5
    - AGD - sudden rise in creat/decreased UO/hematuria/proteinuria

- **High** immunological risk:
  - Definition: Having DSA, PRA (>30) or previously rejected transplant
  - Induction: Antithymocyte globulin
  - Post-Tx: Tacrolimus & MMF
- **Intermediate** immunological risk:
  - Definition: Any degree of HLA mismatch
  - Induction: Steroids (< 2014) and Basiliximab (> 2014)
  - Post-Tx: Azathioprine & Cyclosporine (<2017); Tacrolimus & MMF (>2017)
- **Low** immunological risk:
  - Definition: HLA identical
  - Induction: None (except steroids)
  - Post-Tx: Azathioprine & Cyclosporine

Results:

- 330 renal transplantation
- 105 patients (32%) = early renal biopsy
  - Median age: 39 years (range: 17-62)
  - Male/female: 65%/35%
  - Majority index transplants (95%)

Donors:

- Median age: 34 years (IQR: 14-67)
- 57% males, 43% females
- 70% deceased donations after brain death; 30% living donations
- Overall median CIT: 9 hours (IQR 4-16)
- Donor-recipient race mismatch: 48% of cases

Immunologic risk:

- Average number of HLA mismatches = 5 (IQR 4-7)
- **High** immunologic risk: 23%
- **Intermediate** immunologic risk: 72%
- **Low** immunologic risk: 5%

Biopsy findings:

Result	%
ATN	32%
Acute Rejection	42%
CMR	21%
AMR	16%
Both CMR and AMR	5%
Acute interstitial nephritis	8%
CNI toxicity	4%
Other drug reaction	4%
Pyelonephritis	3%
Granuloma	3%
Other	6%

Biopsy complications:

- 1 X Small bowel perforation
- Arteriovenous fistula in upper pole of the graft
- Abdominal wall pseudo-aneurysm along the biopsy tract

Conclusions

- With current high rate AR, liberal approach to biopsy for EGD remains justifiable
- 2017: Tacrolimus and MMF availability
- 2018: CDC B-cell cross-matching
- Rituximab for prevention of AMR in recipients with a DSA

- More aggressive induction regimens and screening protocols - rate of early AR responsible for EGD may be lower in future
- Re-evaluation of biopsy threshold for EGD may be necessary in future

Acknowledgement of co-authors:

- D Nel, S Poerstamper, S Verhage, C Noel, F Botha, Z Barday, E Muller, T du Toit

Groote Schuur Hospital, University of Cape Town