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## 12-MONTH SURVEILLANCE BIOPSIES IN RENAL TRANSPLANT PATIENTS AT LOW IMMUNOLOGICAL RISK. ARE THEY STILL WORTH OF BEING DONE?

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Background and Aims: In renal transplant field, the progressive increase both of donor and recipient age has led further challenges in patient management. In this setting, the personalization of immunosuppressive therapies (IT) has been strongly suggested. We have investigated renal histology at 12 months after transplantation to assess whether surveillance biopsies (SB) could be considered an additional tool to further improve management of immunosuppression.

**Method:** Monocentric retrospective analysis of SB performed 12 months post-transplant (Tx) between 2009-2018. For each SB were collected recipient and donor demographic data, HLA mismatch, induction and maintenance IT, DGF, cold ischemia time, PRA, DSA and nDSA, previous episodes of acute rejection (AR), serum creatinine (Cr) at the time of SB and 1, 3 and 5 years later, histological score according to Banff classification in force at the time of SB. Statistics included comparison between groups and Cox regression.

**Results:** We analyzed 209 SB in as many pts, most of them at low immunological risk (first Tx in 94.3%, PRA < 30% in 88%, DSA at time of Tx in 5.4%). All pts received induction therapy; maintenance IT included calcineurine inhibitors in 97%, mycophenolate mofetil in 49%, mTOR inhibitors in 30%, azathioprine in 10% and corticosteroids in 33%.

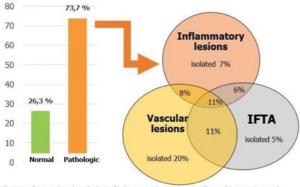
SB showed normal histology in only 26.3% of cases. There were no differences in renal function between normal and pathological biopsies (Cr 1.40 vs 1.46 mg/dl, p=NS). Major histologic findings, isolated or associated with each other [Fig. 1], were vascular lesions (VL, 40%), IFTA (33%) and inflammatory lesions (IL, 32%).

VL correlated with donor age (OR 1.07, p<0.001), whereas IFTA with both donor age (OR 1.03, p=0.04) and DGF (OR 1.07, p=0.04). IFTA was the only histological pattern associated with a lower renal function (Cr 1.58 vs 1.39 mg/dl, p=0.016). IL included interstitial infiltrates (14.8% of specimens), tubulitis (9.6%), glomerulitis (19.6%) and capillaritis (ptc, 13.9%). Both glomerulitis and capillaritis were associated with the presence of DSA, both at Tx (OR 4.35, p=0.037) and at biopsy (OR 5.45, p<0.001).

All types of lesions were found to be related with previous AR (VL with OR 3.08, p= 0.003, IFTA with OR 2.15, p=0.04, IL with OR 4.71, p<0.001) and to be more frequent in the last 5 year biopsies, according to an older donor age (59.5 vs. 52.3 ys, p< 0.001) and a lower HLA-matching (mismatch AB >2: 50.5% vs 32%, p=0.045).

Indipendent histological variables that predicted a worsening of renal function were glomerulitis/capillaritis (HR 6.996, P<0.001) and VL (HR 2.229, p=0.038).

**Conclusion:** Our data confirm that stable renal function does not exclude the presence of subclinical histological lesions, even in patients at low immunological risk. Abnormal findings are present in 73.7% of our SB. Glomerulitis/capillaritis and VL can affected renal function, so their recognition should be considered for immunosuppression optimization. Patients with previous AR are at higher risk for all types of histologic lesions and may require a closer monitoring.



Distribution of normal and pathologic findings at 12-month surveillance biopsies in renal transplant patients.

Figure: