Living=20), HB-EGF mRNA and protein expression were studied at time of donation (T1), after cold ischemia (T2) and after reperfusion (T3). HB-EGF-/- and wild type mice (n=3-5 per group) were subjected to bilateral ischemia (30 min) and sacrificed at 1,5, 6 hrs, 1 after reperfusion to study the role of HB-EGF in renal injury.

Results: In rat IRI, HB-EGF mRNA was 13-fold upregulated (P< 0.01) after 30 min, 90 min and 6 hrs of reperfusion, compared to sham rats. From 1 d onwards, HB-EGF mRNA returned to control levels. HB-EGF protein was expressed in distal tubules. From 30 min after reperfusion onwards de novo expression of HB-EGF was detected in glomerular epithelial cells, proximal tubules and arterial structures. One day after reperfusion the staining pattern of HB-EGF returned to normal. In line with in vivo data, in cultured tubular cells, HB-EGF mRNA was significantly increased (P< 0.05) after 2, 6, 12 and 24 hrs of reoxygenation. In human BD and living donor biopsies, HB-EGF mRNA was significantly increased at T3, compared to T1 (P<0.001). In human sections, predominant tubular expression of HB-EGF shifting from cytoplasmatic expression at T2 to luminal expression at T1 and T3 was found. HB-EGF-/- mice showed significantly less morphological damage after 6 hrs (P< 0.05) and 1 day (P< 0.01) of reperfusion, compared to wild type mice.

Conclusion: Following IRI, HB-EGF is markedly upregulated in rat kidneys, cultured human tubular cells, and human biopsies. Most importantly, HB-EGF-/- mice are protected from renal damage. These results indicate that EGFrec blockers might prove to be protective in the early phase of transplantation.

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545 ASSOCIATION BETWEEN DE NOVO DONOR SPECIFIC HLA ANTIBODY, C4D STAINING IN RENAL GRAFT BIOPSY, AND GRAFT OUTCOME

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Background: Despite improved early graft survival, long-term kidney graft loss rate has not been reduced. Both HLA antibodies and HLA donor specific antibodies (DSA) have been detected and may be causal in chronic allograft nephropathy (CAN) and, especially, in acute rejection. We evaluated the association between DSA, C4d staining in transplant and graft outcome.

Materials and methods: During Sep 2004-Aug 2007, HLA antibody tests usng the Luminex laboratory screen assay system were performed in 348 recipients. Of these, Cd4 deposition was assessed in the biopsies of 69 recipients with transplant dysfunction.

Results: In the 69 cases, 29 (42%) showed C4d negativity, 27 (39%) were Cd4 positive, 6 (9%) were equivocal, and 6 (9%) not diagnostic. Fourty-nine recipients (71%) with transplant dysfunction had HLA antibodies and 41 (59%) had DSA. The proportion of C4d positivity was significantly higher in patients with DSA (Class I only, II only, and I & II) in comparison with patients without post-transplant HLA antibodies (Table). The incidence of graft failure (including current SCr≥4.0) in patients with class II antibodies (Class II only or I & II) was significantly higher than that in patients without post-transplant HLA antibodies (Table). In Figure, grafts of Class II DSA group continued to fail beyond 2 years after transplantation when compared with other 2 groups (None/NDSA or Class I only), however, the difference in graft survival between Class II and None/NDSA group did not reach to statistical significant level (log-rank P=0.32).

Conclusions: Significant association between C4d staining, de novo HLA Class II antibodies and graft failure strongly suggests the importance of post-transplant HLA antibodies. We propose that amelioration of CAN graft loss depends on monitoring and identification of DSA and appropriate immunosuppression of these antibodies.

Table. C4d positivity and graft outcomes according to DSA groups

Antibody Category	N	C4d Positive N (%)	Graft Failure N (%)	Graft Failure or SCr>4.0 N (%)
None (ref)	20	1 (5) (ref)	3 (15) (ref)	5 (25) (ref)
Class I only	10	8 (80) (P<0.001)	2 (20) (P=0.82)	5 (50) (P=0.10)
Class II only	22	13 (59) (P<0.001)	9 (41) (P=0.06)	13 (59) (P=0.03)
Class I & II	9	9 (100) (P<0.001)	4 (44) (P=0.09)	6 (67) (P=0.03)
NDSA	8	2 (25) (P=0.12)	1 (13) (P=0.86)	1 (13) (P=0.40)

Figure. Graft survival according to DSA groups

POSTER BOARD NUMBER P3 – 407

546 COMPARISON OF BIOPSY AND CLINICAL SCORE SYSTEMS TO PREDICT OUTCOME OF EXTENDED CRITERIA KIDNEY DONORS

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Introduction: Advanced age, cerebrovascular death, hypertension, diabetes and low calculated creatinine clearance are all risk factors in deceased kidney donors. Subjects older than 50 with one or more risk factors or subjects older than 65 without any of them are considered as suboptimal or marginal donors and their kidneys all over Italy are rejected or accepted for single or double transplantation following the Biopsy Score proposed by Remuzzi (J Am Soc Nephrol 10,2591,1999). A different Score on simple clinical base has been proposed by Nyberg (Am J Transpl. 3,715,2003). The aim of the present paper is to verify whether the two Score systems can help predict the outcome of renal transplantation.

Methods: We retrospectively analyzed the clinical records of donors and recipients of kidney transplants of the last 4 years. Biopsy and Clinical Score were correlated to the transplant outcome. End points assessed were Early Kidney Function (primary non function, early good function for up to two post-op dialyses or severe post-operative malfunction) and serum creatinine at 1 and 6 months.

Results: In the last 4 years (2004-2007), 271 kidney transplantations were performed at our centre, 151 of them using "ideal" donors and 120 using "marginal" donors (102 as single and 18 as double kidney transplants). In 15 cases both kidneys and in 6 cases only one kidney from marginal donors were discarded owing to a high Biopsy Score; in 3 other cases the organs were discarded because the Biopsy showed a kidney disease. The Clinical Score predicted well the outcome in terms of Early Graft Function and serum creatinine at 6 months (p<0.001). The Biopsy Score did not prove such a correlation since kidneys with 0, 1, 2, 3 or 4 total Score did not result in a significantly different transplant outcome.

Discussion: Up to several years ago, a donor age over 60 and one risk factor were sufficient to discard a kidney. The Biopsy Score era has given an essential contribution to increase the donors' pool with results not as good as ideal donors kidneys, but still widely acceptable. Our study anyhow demonstrates that a simple Clinical Score has a better predictive value of transplantation results and suggests that the Biopsy should be performed in all marginal donors but probably should be interpreted in a less mandatory manner.

POSTER BOARD NUMBER P3 – 408

547 CHRONIC TRANSPLANT GLOMERULOPATHY –; CLINICAL AND PATHOLOGICAL CORRELATES

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Introduction: Chronic transplant glomerulopathy is one of the leading causes of severe post-transplant proteinuria and graft loss. It may develop in a response to several different injurious processes, such as humoral rejection or thrombotic microangiopathy. In the majority of cases the etiology is obscure, which excludes the possibility for targeted intervention. Our current knowledge about risk factors for the development of TG, as well as factors affecting its dynamics and prognosis is poor.

The aim of the study was to find pathological and clinical risk factors and correlations of TG as well as parameters that influence the survival of grafts with that pathology.

Materials and methods: We retrospectively reevaluated all 86 kidney transplant cases with TG that have been recognized on the basis of indication